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Editorial

During the course of past ten years, the international community has continually given priority to responding to HIV/AIDS as part of commitments to achieve global health goals. At the United Nations General Assembly High-Level Meeting on AIDS in 2006, countries including SAARC Member States committed to work towards Universal Access to comprehensive HIV prevention, treatment, care and support by 2010.

Universal Access is the promise of commitment to provide HIV prevention, treatment, care and support for all those who need it. Achieving Universal Access is a critical mid-way point to reach the Millennium Development Goal to "halt and reverse the HIV/AIDS epidemic". Universal access signifies both a concrete commitment and a renewed resolve among people all over the world to reverse the course of the HIV epidemic. It is a process that builds on past initiatives and infuses existing efforts with greater momentum. Universal Access does not imply that there will be, or should be, 100% coverage of HIV prevention, treatment, care and support services. However, the world has committed to make concrete, sustained advances towards high-level of coverage for the most effective programmes needed to manage diverse epidemics in all regions. The basic principles for scaling up towards Universal Access emphasize that services must be equitable, accessible, affordable, comprehensive and sustainable over the long term.

Different countries including Member States of the SAARC Region have diverse HIV epidemics and often have distinctly different needs. Therefore, each country will adopt varying time lines and strategies to achieve scaling up of services. Except Afghanistan and Bhutan, other Member States of the SAARC Region target the universal access to prevention and treatment by 2010. In addition to that, Nepal has also targeted to achieve the universal access to care and support by 2010. However, the Member States need to achieve high coverage for programmes addressing the most at risk populations. By setting national targets, Member States are making efforts to reach Universal Access within the time frame and that will set them on the way to reach the 2015 Millennium Development Goal to "halt and reverse the HIV/AIDS epidemic".

Access to antiretroviral [ARV] treatment continues to expand at a rapid pace in low and middle income countries during the year 2008. More than 4 million people in low and middle income countries were accessing ARV treatment in the year 2008. Approximately 565,000 people received ARV in the East, South and South-East Asian Region in 2008 scaled up from 420,000 in 2007, a 35% increase over the previous year and an eightfold increase since 2003.

At the end of December 2008, 238,000 [214,000 – 263,000] people living with HIV/AIDS were receiving ARV treatment in the SAARC Region, achieving a coverage of 31% [25% - 39%] of estimated number of those who need the treatment.

UNAIDS has identified nine priority areas for its support to countries to achieve their Universal Access targets. They are reducing sexual transmission of HIV, Preventing mothers from dying and babies from acquiring HIV infection, Ensuring that people living with HIV receive treatment, preventing people living with HIV from dying of tuberculosis, protecting drug users from acquiring HIV, removing punitive laws, policies, practices, stigma and discrimination that block effective responses to HIV/AIDS, empowering young people to protect themselves from HIV, stopping violence against women and girls and enhancing social protection for people infected and affected by HIV/AIDS. These areas will contribute both to achieve targets of Universal Access and enable advancement to the Millennium Development Goals.

Achieving country defined targets by 2010 presents an opportunity to change the pace of the response to HIV/AIDS epidemic. It will save lives, protect babies and young people from getting infected and ensuring that orphans have access to quality education. Achieving Universal Access will also have a significant impact on broader health and development goals such as maternal mortality, poverty and gender equality. It will also contribute to the strengthening of health systems and increasing human resources.

Hence, this worldwide movement towards Universal Access aims not only to contain the epidemic, but to mark the beginning of the end of the spread of HIV.

COMMUNITY BASED RISK BEHAVIOUR STUDY ON HIV/AIDS TARGETING WOMEN IN NEPAL -2007

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ABSTRACT

Nepal has progressed from a HIV low prevalence country to one with a concentrated epidemic in certain subgroups of population. It has been documented that girls and women are more vulnerable to HIV infection. However there is little documented evidence on the risk behaviour among women in Nepal. This study was conducted to assess the pattern of risk behaviour for HIV among women in Nepal.

Methodology : The main component of the study comprised a community based cross- sectional study, using a multi stage random sampling technique. Data was collected by trained field health workers using an interviewer administered questionnaire. Eight focus group discussions were also conducted to supplement the findings. Statistical analysis was carried out using SPSS version 13.

Results : A significant number of un married (13.7%) women and 2.2% of married women indulged in high risk sexual behaviour. A significant positive association was observed between sexual risk behaviour of married women and monthly family income less than 5000 Nepali Rs ,age group 25-34y and young age group (15- 34) in unmarried women. Nearly 70% of participatory women have heard about AIDS and have satisfactory level of knowledge about HIV/AIDS. However, significant number of respondents had misconceptions that one could contract HIV through hand shaking, mosquito bites and hugging. Using Condoms during unprotected sexual intercourse in both married and unmarried women were low (19.4% and 6.2% respectively). Findings of Focus Group Discussions revealed there is a strong stigma associated with HIV/AIDS in this rural community in Nepal.

Conclusions : One in every seven unmarried woman in Nepal indulged in high risk sexual behaviour, which is much more compared to married women. There is an urgent need for reproductive health education especially among teenagers and for the National HIV/AIDS Control Programme to expand its awareness generation activities.

Keywords : HIV/AIDS, women, risk behaviour, Nepal

INTRODUCTION AND JUSTIFICATION

It has been documented that girls and women are more vulnerable to HIV infection and its impact. Globally, more than half of persons living with HIV are females, a sharp contrast to the early stages of the epidemic, when AIDS was thought a disease mainly striking men. Women are vulnerable to HIV infection in many ways. Evidence suggests that large share of new infections is due to gender – based violence in homes, schools, the workplaces, and other social arenas.[1] Forced or coerced sex renders a woman even more vulnerable to infection; the younger she is more likely it is that she will contract HIV.

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In the Human Development Report 2001, Nepal features among the economically poorest countries in the world.[2] Nepal's social indicators remain well below the average for the South Asia region: More than 40 percent of the Nepalese population lives below the national poverty line and nearly 60 percent of all adults are unable to read or write. Additionally, women have traditionally a lower status than men and gender inequality is deeply rooted.[3] Nepal is one of the few countries worldwide in which men live longer than women. More boys than girls receive any form of education, women generally work longer hours than men, and men have better access to services, including health. In Nepal, the topography, environmental degradation, poverty and economic migration are all linked and they combine with other factors to increase vulnerability to HIV/AIDS.

The first HIV infection in Nepal was identified in 1988. Nepal's HIV epidemic is largely concentrated in high-risk groups, especially sex workers (SW) and Injecting Drug Users (IDUs). Injection drug use appears to be extensive in Nepal and to significantly overlap with commercial sex. Another important factor is the high number of sex workers who migrate or are trafficked for work, thereby increasing HIV prevalence in the sex workers' network in Nepal more rapidly. There are many risk factors that put Nepal in danger of experiencing a widespread epidemic. Some of these include cultural, social and economic constraints to condom use, especially with commercial sex workers, and large number of internal and external migrants within Nepal and neighboring countries.

By 2007, the number of People Living with HIV/AIDS (PLHA) in Nepal was estimated at 70,256 persons. As reported to the National Centre for AIDS and STD control (NCASC), Teku, Kathmandu, Nepal and the cumulative number of HIV positive cases including AIDS as of April 2008, was 11234. Among them 68.1% were males and 31.9% were females. Out of total HIV positive cases, 1754 were full blown AIDS cases. 232 new cases were added with in April 2008.[4]

Disease is affecting mainly the people in sexually active age group of 15-49 years. Nearly 92.2 % of the cases are in the age group of 15-49 years . About 46.6% of the reported HIV positive cases belong to clients of sex workers followed by Housewives (22.0%), IDUs (19.0%) and Sex Workers (7.0 %). This shows that the number of infected housewives is about three times higher than the number of sex workers.[4]

According to the above epidemiological data Nepal is facing rapid increases in HIV prevalence among high risk groups such as sex workers and injecting drug users. Nepal's poverty, political instability and gender inequity, combined with low levels of education and literacy make the control task more challenging. In addition prevailing denial, stigma and discrimination that surround HIV/AIDS, make this task more difficult. In addition Nepal's HIV epidemic is largely concentrated among high-risk groups, especially female sex workers (FSW) and IDUs, and currently the, problem is increasing among migrants and men having sex with men (MSM). Most of them do not know that they are infected and may be engaging in unsafe sexual practices.[5] Above demographic and epidemiological findings shows that women in Nepal are vulnerable to HIV infection. Studies on risk behavior on HIV/AIDS targeting women in Nepal are limited. Therefore this study was conducted in Nepal to achieve the following objectives. To identify the risk behavior of Nepalese women in relation to acquiring HIV infection.and to assess the pattern of sexual and other risk behaviour for HIV among women in Nepal.

METHODOLOGY

Study Design :

This study consisted of two components

(a) Community based descriptive study
(b) Qualitative component- Focus Group Discussion

Study Setting :

Nepal comprises of 5 development regions, seventy five districts and 26 Million populations (2004). Geographically, Nepal is dividing into three major areas.

1. Himalayan Area (Mountain)
2. Hilly Area
3. Plain Area (Terai)

Primary stratification was done based on these geographical regions. However, Himalayan area is excluded from the study because of its difficult terrain. Hence, this study was conducted in randomly selected four (4) districts, two from Hilly and two from Terai areas of Nepal, namely Gorkha, Kaski, Parsa and Banke districts.

Study Population :

The study population comprises females who are residents of these four districts. The following females were excluded from the study:

- Those who refused to give consent for the study.
- Visitors from other areas (Those who are residing in these areas for less than 6 months).

All women irrespective of their HIV status were included into the study.

Sample Size :

The sample size in a behavior study depends on the population size and the frequency of the behavior risk condition to be measured. Since there is limited data regarding risk taking behavior for Nepalese, in the present study only the population size was considered when calculating sample size. (10% of the female population was taken).[5] Considering above factors a sample of 5423 women permanently residing in study districts was selected.

Data collection procedure :

In the Wards (village) the first house was randomly selected by the Principal Investigator (STAC staff member) and address was given to relevant Interviewers. Starting from that house interviewer visited each house, which is situated on the right side of the main entrance of that particular house. Like wise required number of females from each village according to the sample size were enrolled and interviewed.

The interviewer visited the houses and enquired whether an eligible woman is residing in the house. If such a woman is present and gave consent, she was enrolled as the first respondent. From there onwards, the interviewer visited the houses as per defined methodology until required numbers of females were enrolled and interviewed. If there were more than one females in a house, all eligible females were selected for the study.

Study Period : 4 months starting from September 2007.

Study Instrument :

The study instruments were

(1) Interviewer Administered Pre Coded Structured Questionnaire.

(2) Focus Group Discussion : Focus group discussions were employed in each selected district in coordination with district public health office with targeted population involved in different occupations to explore the factors placing them at risk for engaging in HIV risk behaviors and to identify barriers on involving into healthy behaviors.

Formulation of Questionnaire :

Simple and clear colloquial language was used in the formulation of questions. A single variable was measured from each question. Questionnaire consisted of following components

- Demographic data
- Mobility
- Sexual risk behavior
- Risk of injecting drugs
- Knowledge about HIV/AIDS

Pre Testing Of Questionnaire :

Pre testing of questionnaire was carried out to determine the acceptability, comprehension and ease of administration of the questionnaire. It was pre tested among the adult females in the Kathmandu Valley.

Selection and Training of Field Staff :

Female Community Health Workers (FCHW) were selected as field investigators to assist the Principal Investigator in data collection. They were selected from the same village. Two days training were given to them prior to data collection by the STAC staff.

Ethical Consideration :

The following ethical issues were considered in the design of the study.

- The participants were briefed regarding the nature, objectives, and method of the study and their voluntary participation acquired.
- Participants were given free option to withdraw from the study at any point of time.
- The identifiers were not recorded on the questionnaire
- Permission was obtained from relevant authorities before commencement of the study

Analysis of Data :

Statistical analysis was performed by STAC staff using the Computer Programme Statistical Package for Social Science (SPSS) 13 Version.

Qualitative research component- Focus Group Discussions

Eight Focus Group Discussions were completed, two from each districts of target groups .The focus group discussion began with the presentation of a story about a woman with history suggestive of AIDS. The story followed the women throughout the stages of her illness until she became a HIV positive and how her family and the community may respond. This approach allowed participants to speak in the third person about a fictional woman with HIV infection and not feel like the story and their view were reflections of their own thinking.

Participants were then asked :

- ✓ What is the risk behaviour in that study?
- ✓ Reasons why people are not using condoms?
- ✓ What is the reaction of her (fictional woman) immediate family members and society?
- ✓ How did she (fictional woman) develop the disease?
- ✓ What precautions she (fictional woman) must have taken
- ✓ Stigma related to HIV/AIDS
- ✓ Knowledge about HIV/AIDS
- ✓ Other related issues like avaialability of reproductive services, unwanted pregnancies etc

RESULTS

A total of 5423 both married and unmarried women were interviewed .Majority of women belonged to 15-24 y age group followed by 25 -34 year age group.Mean age of study population is 27 years.In the study population about 75 percent were married and living with spouse at the time of the survey.Respondents who never married accounted for 20%.Majority (82%) of the respondent were Hindu by religion. Nearlry 22% of study population were illiterate. The distribution of literate study population by completed number of years of education reveals that majority (59%) had only primary education.Only 15 women had education up to graduate or post graduate level.Overall, 41 percent of study population was employed at the time of survey. Only 2% of the respondents reported that they were away from home during the last 12 months for occupation.

Table 1. Socio – Demographic characteristic of study sample

	Study population (n- 5423)	
Age group (in years)	Number	%
15 – 24	2574	47.5%
25 -34	1716	31.6%
35 -44	864	15.9%
> 45	269	5%
Mean age – 27 years, SD-8.4 years		
Religion		
Hindu	4448	82%
Non-Hindu	975	18%
Literacy		
Literate	4235	78.1%
Illiterate	1188	21.9%
Educational status		
Primary	3200	59.0%
Secondary	1020	18.8%
Graduate	12	0.22%
Post graduate	3	0.06%
Illiterate	1188	21.9%
Marital status		
Never married (Single)	1088	20.1%
Currently Married(Living with husband)	4083	75.3%
Currently Married(Not living with husband	139	2.6%
Divorced	29	0.5%
Widowed	82	1.5%
Living with partner (But not married)	2	0.04%
Whole family income (NRs)/month		
< than 2500	1469	27.1%
2500 – 4999	1751	32.3%
5000 – 9999	1391	25.7%
> than 10000	812	14.9%
Current occupation		
House wife	3208	59.2%
Agriculture	607	11.2%
Student	846	15.6%
Business	466	8.6%
Migrant labour	26	0.5%
Other	270	4.9%
Last one year away from home for occupation		
Yes	107	2%
No	5316	98%

Husbands educational status (n-4333)		
Primary	1986	45.8%
Secondary	998	23.0%
Graduate	49	1.1%
Post graduate	38	0.9%
Illiterate	1081	24.9%
Don't know	181	4.2%
Husband's migration for job (last one year) (n-4333)		
Yes	1625	37.5%
No	2708	62.5%%

The study revels that comparatively more men (24.9%) were illiterate as compared to women (21.9%).Nearly 38% of respondendents reported that their husband were away from home during the last one year for occupation (Table 1).

(C) Sexual risk behaviour (Married women)

This study revealed that 2.2% of married women indulge in extramarital sexual act during last one year. Those who had extramarital partners 73% had a only one partner , 19.4% had two partners and seven women (7.5%) stated they had 3 or more than 3 sexual partners (Table 2).

Table 2 : Distribution of married women who ever had another sexual partners, number of partners and condom use by husband and partnerrs

Sexual partners other than husband	Number	%
Yes	93	2.2%
No	3990	97.8%
Number of partners (n -93)		
One	68	73.1%
Two	18	19.4%
Three or more	7	7.5%
Condom use while having sex with partner (n-93)		
Yes	18	19.4%
No	60	64.5%
Some times	15	16.1%
Condom use while having sex with husband (n-3817)		
Yes	374	9.8%
No	3015	79.0%
Sometimes	428	11.2

This population based survey has also made an attempt to assess the proportion of women who were using condoms while having sex with husband and partners.It was found that nearly 19% of extra marital partners and 9.8% of husband's regularly use condoms while having sexual intercourse.

Table 3: Reasons for not using condoms while having sex with husband / partner

Reasons for not using condoms	With husband (n = 3015)	With Partner (n = 93)
Not available at the time of intercourse	245 (8.1%)	26 (43.3%)
Not aware about the importance of the condom	1769 (58.7%)	11 (18.3%)
Husband/partner not likes to use condoms due to diminished sexual sensation	2513 (83.3%)	46 (76.7%)
Cannot negotiate with the husband	711 (23.6%)	36 (60.0%)
Problems of disposing condoms	26(0.9%)	2 (3.3%)
Using other family planning methods	2678 (88.8%)	-

The reasons for not using condoms by husband and partners were assessed. Majority stated that husband/ partner dislike using condoms during sexual intercourse because of diminished sexual sensation. Other common reasons stated were, using other forms of family planning methods , cannot negotiate with the partner and not aware about the importance of the condom (Table 3).

(D)Sexual Risk Behaviour of un married women (n=1088)

This study revealed that out of 1088 unmarried women 149 (13.7%) of females are indulged in premarital sex (Table 4). Approximetely 24% of unmarried women who were expeinced sexual activity, had started sexual activity before the age of 15 years (Table 5). It was found that 81.5% of unmarried women who had a penetrative sex with a partner during last week did not use condoms (Table 5). About 45.5% of these women have mentioned that they are not aware about the importance of the condoms (Table 6).

Table 4 : Distribution of unmarried women indulged in pre marital sex		
Life time sexual experience of unmarried women	Number	%
Yes	149	13.7%
No	939	86.3%
Total	1088	100.0%

Table 5:Selected charcteristics of unmarried women who experinced sexual risk behaviour (n-149)		
Age at first intercourse	Number	%
15y and Less than 15y	36	24.1%
More than 15 years	113	75.9%
Having current sexual partner		
Yes	48	32.2%
No	101	67.8%
Routes of practising sex		
Vaginal	27	93.1%
Oral	19	65.5%
Anal	6	20.7%
Extra Vaginal	20	69.0%
Condom used during vaginal intercourse (n-27)		
Yes	2	6.2%
No	22	81.5%
Some times	3	11.1%

Table 6:Reasons for not using condoms (Unmarried Women): (N=22)		
Reasons for not using condoms -Partner	No	%
Not available at the time of intercourse	14	63.6%
Not aware about the importance of the condom	10	45.5%
Partner not likes to use condoms	19	86.4%
Cannot negotiate with the Partner	5	22.7%

(F)Knowledge about HIV/AIDS.

On an average 70% of women were aware of HIV/AIDS and condoms.A vast majority of the respondents knew that HIV could be transmitted through unprotected sexual intercourse (84%) followed by other correct response like infected blood (66%) and mother to child transmission (84%).On the contrary a significant number (52%) had the misconception that one could contract HIV through shaking hands with HIV infected person. A further 24% believed that they might get infected by mosquito bites.

Table 7: Distribution of respondents by their main source of information on HIV/AIDS	
Main source of information	Number
Television	3036
Radio	3126
Newspaper	1876
Other printed materials	658
Heath workers	1356
Parents	15
Teachers	47
Friends	2987

It has been found that television,radio,friends, news paper and health workers were the major source of information for the knowledge about HIV/AIDS (Table 7).

Section G :

In this study sexual risk behaviour is defined as those women indulging pre marital and extra marital penetrative (vaginal/anal) sexual intercourse.

Table 8 : Association between sexual risk behaviour of married women and some socio-demographic variables:				
	Sexual risk behaviour of married women			
Age group (in years)	Yes(%)	No(%)	Total	Crude Odds Ratio &CI
15 – 24	23 (1.2%)	1851 (98.8%)	1874	1(Reference)
25-34	45 (3.3%)	1301 (96.7%)	1346	2.7(1.6-4.4)
35-44	18 (2.3%)	775 (97.7%)	793	1.9(1.0-3.5)
>45	07 (2.8%)	242 (97.2%)	249	2.3(0.9-5.6)
Income				
Less than NPR 5000	64 (2.6%)	2376 (97.4%)	2440	OR =16.7, CI= 9.9-27.1
More than NPR 5001 (Reference)	29 (1.6%)	1793 (98.4%)	1822	

Literacy status				
Illiterate	63	3183	3246	OR-0.7,CI-0.5-1.1
Literate	30	986	1016	

Table 9: Association between sexual risk behaviour of un-married women and some socio-demographic variables:

	Sexual risk behaviour of un-married women			
Age group (in years)	Yes	No	Total	Crude Odds ratio (CI)
15 – 24	88 (16.4%)	450 (83.6%)	538	2.2(1.4-3.4)
25-34	29 (17.8%)	134 (82.2%)	163	2.4(1.3-3.8)
35-44	30 (8.2%)	338 (91.8%)	368	1 (Reference)
>45	02 (10.5%)	17 (89.5%)	19	1.3(0.3-5.8)
Income				
Less than NPR 5000	96	650	746	$X^2 = 1.4$ ($p > 0.05$)
More than NPR 5001	53	289	342	
Literacy status				
Illiterate	127	816	943	$X^2 = 0.3$($p > 0.05$)
Literate	22	123	145	

Twenty five years to 34 years married women group had a 2.7 times higher risk of indulge in risky sexual behaviour compared to the married women with 15-24 years. This association was statistically significant. There was a significant positive association between younger age group (15-24 and 25-34) and sexual risk behaviour in un-married women.

There was a significant positive association between low income group and sexual risk behaviour in married women. There is no statistically significant association between income and risk sexual behaviour in un -married women.

There is no statistically significant association between literacy and risk sexual behaviour in both married and unmarried women.

Section H :Findings of Focus Group Discussions:

Knowledge, Beliefs and Perception about HIV/AIDS

Unmarried participants demonstrated a general basic knowledge of the HIV/AIDS. The knowledge of married women was poor.

Most participants agreed that men are more frequently infected with the disease. The reasons given were that men are more mobile and they are not using condoms while indulging in unsafe sex.

Most married women stated that their husbands are not using condoms during intercourse. Reasons for not using condoms given by participants were

- ✓ Condoms are expensive
- ✓ Not available at the time of intercourse
- ✓ Husbands do not like to use.

Knowledge and practices regarding Intra venous Drugs usage was extremely poor amongst all the participants in the FDGs. This practice is rare in this community.

Majority of participants stated, having sex with migrant persons like truck drivers without using condoms, was the major risk factor by which one can get HIV infection.

Accessibility of education and Health care for women:

When asked about where most people received their information about HIV/AIDS, health education sessions held by government health staff was mentioned the most. Some participants learned about the disease from Radio and TV, neighbours and relatives. Very few mentioned the bill boards as a source of information.

Stigma related to HIV /AIDS:

When we asked if someone gets (fictional woman) infected with HIV what action they have to taken. Some participants mentioned tendencies of women to hide their disease status because they would not want to upset their family life. These hiding tendencies occur because women fear that if the family (especially husband) and community learn that she has HIV infection then she will be a shamed and ignored or ostracized by the family members and community.

Discussion :

According to our knowledge this study seems to be the first of its kind in Nepal that attempts to understand sexual risk behaviour and risk perception in relation to HIV/AIDS of women in the country. It begins to address a severe dearth of information, particularly on high-risk sexual behaviour among the women of the country.

The study has shown that substantial proportions of young unmarried women and nearly 2% of married women indulge in high risk sexual behaviour.Early sexual experimentation, multiple partners and irregular use of condoms,are common . Knowledge of condoms seems to be superficial and information regarding the risk of unsafe sex and its consequences is inadequate.

Throughout history, societies have dealt with the problem of premarital sex and illegitimacy by strictly supervising young people so that sexual activity does not begin until marriage.[6] Although premarital sex is socially unacceptable in Nepal, the study has shown that the proportions among sexually experienced unmarried women are quite high.

The findings of the study have some important programme implications. Women are aware of some forms of protection from HIV/AIDS and other reproductive risks in general. However, their information is incomplete and they hold a number of misconceptions. Therefore action is needed to dispel such myths and misconceptions and impart more knowledge of contraception especially condoms.

Socioeconomic Status :

As expected, a majority (82%) of the women were Hindu. In this study 20.% were never married. Less than 3 percent of the respondents reported separation from their spouse. The divorce rate of study population was very low (0.5%) .This may be due to socio-cultural practices prevailing in the SAARC region especially Nepal where divorce is unacceptable by the society. This pattern of literacy (78%) is higher than 2001 census in Nepal, where adult female literacy rate of Nepal was 56.7%.However, the majority of the literate women (59%) had received only primary education. Majority of women level of monthly income less than 5000NRs (70US$). Majority of women are house wives (59%).Others are involved in various occupations such as agriculture, industrial, business, uniformed services, etc

Sexual risk behaviour : married women

It was found that 2.2% of the adult married females indulge in extra marital sexual activities. Out of this number (93) 27% of women stated that they had a sexual relationship with multiple partners which is a high risk for HIV/AIDS.It is alarming that more than 80% of married women,are not regularly using condoms during intercourse with partners other than husband.

Even though less number of married women reported high risk sexual behaviour in this study, they are at greater risk of getting HIV or other STIs due to transmission from an infected spouse. The results show 37.5% of married men were currently working in other countries during last 12 months.This fact is consistent with findings of other studies in Nepal. The men subsequently obtain the services of HIV infected Commercial Sex Workers (CSW).[7] They then return home, transmitting the virus to their unsuspecting wives , who subsequently pass the virus to their unborn children.In a study conducted by Beine in the village of Saano Dumre, Nepal revealed 56% of the men were reported to be working either in India or further abroad.

Sexual risk behaviour: un- married women.

Although premarital sex is socially unacceptable in Nepal, this study revealed that out of 1088 unmarried women 149 (13.7%) of females are indulged in premarital sex. It is alarming that 81.5% of unmarried women who had a penetrative sex with a partner during last week did not use condoms. About 45.5% of these women have mentioned that they are not aware about the importance of the condoms. This highlights the importance of condom promotion programmes to youths especially school dropouts by National AIDS control programme and other non government organizations working in the field of HIV/AIDS. Those who indulge in sex , one fourth stated their sexual activity started before the age of 15 years. The first sexual event has clear health implications, since it marks initiation into the sexual act, which is unprotected, and carries a risk of adverse outcome such as unplanned pregnancy and sexually transmitted infection.[8] Government and non government authorities must address this issue carefully.

A study conducted among young factory workers in Nepal revealed that one in every eight unmarried girls (13%) had an experience of sexual intercourse prior to the date of survey.[9] Our study also revealed similar findings (13.7%). In a recent study among male and female students in Pokhara , Nepal it was discovered that one third of students were sexually active and that the average age of first sexual experience was between 14 and 17.[10] Other studies have also confirmed similar low ages for reported first sexual contact.[11]

Knowledge about HIV/AIDS and use of condoms.

Knowledge about STDs and HIV/AIDS is often considered to be associated with the behaviour. However, the link between knowledge and behaviour is not automatic; the

former does not always affect the latter.[12] For example, a Korean study involving male students and industrial workers found that a large majority of respondents (99% of students, 96% of industrial workers) knew that AIDS could be transmitted by sexual intercourse with an infected person. At the same time, more than 9 out of 10 young men in both groups knew about condoms both as a method of contraception and as a means of preventing STIs. However, of those who were sexually active, only 39 % of industrial workers and 48% of students reported they have used condom in their last sexual intercourse.[13] Our study findings revealed the similar findings where on an average 70% of women were aware of HIV/AIDS and condoms.A vast majority of the respondents knew that HIV could be transmitted through unprotected sexual intercourse (84%) followed by other correct response like infected blood (66%) and mother to child transmission (84%).On the contrary a significant number (52%) had the misconception that one could contract HIV through shaking hands with HIV infected person. A further 24% believed that they might get infected by mosquito bites. These findings indicate the need for proper health educational programmes to women by National AIDS control programme. In spite of fair knowledge about HIV/AIDS, only 9.8% were using condoms during sexual intercourse. The reasons for not using condoms were assessed. Majority stated (83.3%) that husband/partner dislike using condoms during sexual intercourse because of diminished sexual sensation. Similar finding was reported in the study done by Abdullalla et al (2002).[14] Other reasons stated were, using other forms of family planning methods and not aware about the importance of the condom. Compared to the married women, the percentage of inconsistent condom users was low among unmarried women (80.6%).Like married women, most common reasons for not using condom among unmarried women was partner does not like to use condoms. Only 18% of unmarried women stated that they were not aware about the importance of the condoms. Hence, risk reduction targeted interventions including condom social marketing should be geared for sexually active community members especially for unmarried persons by the National AIDS Control Programme or other organizations. In addition, condom is an effective contraceptive with dual protection and it has hardly any side effects. Of the respondents who received information on HIV/AIDS , the mostly cited sources of information were health workers,Television and Radio. The findings of the present study were compatible with the findings of the study conducted in other countries in the region.[15]

Association between Sexual risk behaviour and other variables:

1. Age.

A significant finding in this study was that there was a positive association between young age group and sexual risk behaviour of unmarried women.

The present study was conducted in the main cities of Nepal. Owing to poverty and unemployment in rural areas, migration of young boys and girls aged 19 years and under, especially to main cities located in the region, is very high. According to UNICEF, approximately 200,000 young people (10-19 years) migrate to urban areas in Nepal. In addition, the rapid growth of formal manufacturing sector in Nepal has led to a large influx of young people from rural areas seeking employment in major cities.Many of these young people arrive in the city unaccompanied by parents or other guardians. Owing to poor parental supervision, unmarried women may start sexual experimentation at younger ages and have more exposure to casual relationships.

2. Monthly household income.

In married women, monthly household income less than 5000 NRs are significantly associated with indulging risky sexual behaviour. This is an another study heighlighted HIV infection is closely associated with poverty.[16] Dixit (1996) also concludes that " poverty is the root cause of the problem of AIDS".[17] Another study of STD/HIV infection among prostitute in Calcutta (based on self reporting) found that extreme poverty, illiteracy and family disturbances were among the factors most responsible for leading them into prostitution.[18]

In the present study, when considering the attitudes towards some aspects of HIV/AIDS at the Focus Group Discussions, the respondents of all 4 areas had unfavourable attitudes towards patients affected with AIDS and other STIs and had discriminating views towards commercial sex workers, girls working in 'Dance Clubs", homo sexual and IV drug users. The respondents were of the view that these groups were solely responsible for the spread of HIV/AIDS. Study done in Sri Lanka in 1992 on a national scale obtained consistent result with the present study with more than 50 % of respondents having discriminatory views towards patients with AIDS.[19]

Questioning sexual behaviour in a rural setting in Nepal is a challenge. However one of the goal in HIV / AIDS educational programmes is to promote the use of preventive behaviour. Findings of the present study can effectively be used to prevent HIV/AIDS in Nepal, in future.

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PERCEPTION AND KNOWLEDGE ABOUT HIV/AIDS AMONG STUDENTS IN A MEDICAL COLLEGE IN WESTERN NEPAL

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ABSTRACT

Background : Medical students are taught about HIV/AIDS throughout the curriculum. The objectives of the present study were:

a) To study the perceptions and knowledge of medical students regarding HIV/AIDS
b) Obtain information on lacunae observed and.
c) Compare the median scores among different subgroups

Methods : The study was carried out among the first, third, (preclinical) and fifth and sixth semester (clinical) students at the Manipal College of Medical Sciences, Pokhara, Nepal. The students were explained the objective of the study and invited to participate. Written informed consent was obtained. Student perception regarding HIV/AIDS was studied by noting their degree of agreement with a set of 22 statements using a modified Likert-type scale. The median score was compared among different subgroups.

Results : 163 students participated. The median score was 77 (maximum score 110). The median score was significantly higher among Nepalese students compared to other nationalities (p=0.000) and among the scholarship students compared to the self-financing (p=0.000). The free text comments stressed the importance of safe sex in controlling HIV/AIDS.

Conclusion : The overall scores were high. The lacunae observed can be addressed through educational interventions. The foreign and the self-financing students need greater training to tackle HIV/AIDS. The study had many limitations which may affect its generalizability and representativeness and more detailed studies are required.

Key words : HIV/AIDS, Knowledge, Medical students, Nepal, Perceptions

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) was first diagnosed in the United States (US) in 1981; over 90% of all infected cases occur in developing countries and the number of cases is increasing every year.[1] AIDS can provoke irrational emotions and fears in healthcare providers, including medical students. These fears may act as barriers to successful educational efforts about the diseases and lead to adverse outcomes.[2] In Nepal, limited data indicate that Human immunodeficiency virus (HIV) prevalence is around 0.5 percent in the adult population between the ages of 15 –49 with a male female ratio of approximately 3:1.[3]

HIV/AIDS is becoming an important problem in Nepal and South Asia. Young and productive age groups of the population are at the center of the HIV epidemic in Nepal.[4] Since 1997, the disease has been spreading rapidly among intravenous drug users and commercial sex workers. The

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author had called for a national response in terms of both HIV prevention and care.[5] There was a violent ten-year conflict in Nepal. The authors of a recent article state that the violent conflict may have fuelled the HIV/AIDS epidemic in Nepal.[6]

The Manipal College of Medical Sciences (MCOMS), Pokhara is affiliated to the Kathmandu University for the undergraduate medical (MBBS) course. The college admits students from Nepal, India, Sri Lanka and a few students from other countries. The basic science subjects are taught during the first four semesters and the clinical subjects from the fifth semester. HIV/AIDS is covered in an integrated manner during both the basic science and clinical semesters. Medical students as future doctors will play an important role in caring for HIV/AIDS patients. Also medical students belong to the young and vulnerable age group of the population and their behavior may put them at risk of HIV/AIDS and sexually transmitted diseases. Knowledge and perceptions of students about HIV/AIDS should be assessed so that appropriate changes in the teaching-learning methodology can be carried out, if needed.

Hence the present study was carried out with the following objectives.

a) To study the perceptions and knowledge of medical students regarding HIV/AIDS
b) Obtain information on lacunae observed so that appropriate teaching-learning programs can be initiated and
c) Compare the median scores among different subgroups

METHODS

The study was carried out among first, third, fifth and sixth semester undergraduate medical (MBBS) students at the Manipal College of Medical Sciences, Pokhara, Nepal during the month of July 2008. The first and third semester students were in the Basic Science years while the fifth and sixth semesters were in the clinical years. The study were explained the objectives of the study and invited to participate. Written informed consent was obtained from all the study participants.

Basic demographic information like gender, nationality, semester of study, occupation of parents, method of financing of medical education and whether the student hailed from an urban or rural area were noted. Perception and knowledge about HIV/AIDS was obtained by noting the respondents' degree of agreement with a set of 22 statements using a modified Likert-type scale. The statements dealt with general information about HIV infection, prevention of infection, diagnosis and treatment. The questionnaire used is shown in the Appendix. Statements 2, 3, 4, 6, 7, 8, 12 and 17 were negative and their scores were reversed to calculate the total score.

The median total score was calculated. The median scores of individual statements were also worked out. The median total score was compared among different categories of respondents. Mann-Whitney test was used for dichotomous variables and Kruskal-Wallis test for the others. A p value less than 0.05 was taken as statistically significant. Free text comments were invited from the respondents and the common comments were noted.

RESULTS

A total of 163 students participated in the study. The total number of students in the four semesters was 275 giving a response rate of 59.3%. Twenty-eight students were from the first semester, 50 from the third, 47 from the fifth and 37 from the sixth semester participated. The response rates of the first semester was 56% (28 of the 50 students), of the third semester was 66.6% (50 of the 75 students). For the fifth and sixth semester the rates were 62.7 and 49.3% respectively.

Table 1 shows the demographic characteristics of the respondents. Nepalese and Indians were the major nationalities. Male students were more and few students had doctor parents. Majority of students were self-financing.

Table 1: Demographic characteristics of the respondents

Characteristic	Number (%)
Semester of study First	
Third	28 (17.2)
Fifth	50 (30.7)
Sixth	47 (28.8)
	38 (23.3)
Nationality	
Nepalese	75 (46)
Indian	64 (39.3)
Sri Lankans	16 (9.8)
Others	3 (1.8)
Gender	
Male	108 (66.3)
Female	48 (29.4)

Occupation of father	
Doctor	39 (23.9)
Others	114 (69.9)
Occupation of mother	
Doctor	17 (10.4)
Others	40 (24.50
Housewife	97 (59.5)
Method of selection	
Govt. selected	50 (30.7)
Self-financing	106 (65)
Place of origin	
Urban	126 (77.3)
Rural	21 (12.9)

The median total score was 77 (maximum possible score 110). The interquartile range was 11. Table 2 shows the median total scores of individual statements. Many respondents were under the impression that HIV/AIDS is a more dangerous disease than hepatitis B. The respondents were equivocal about the statement 'HAART is effective in treating HIV/AIDS' and about enrolling them and their family enrolling children in a school which admits HIV-positive children. They were in agreement that homosexuality was a crime against God and humanity. The scores of statements 18, 19 and 20 were very high.

Table 2 : Median scores of individual statements

Statement number	Median score
One	Four
Two	Four
Three	Four
Four	Two
Five	Four
Six	Four
Seven	Four
Eight	Four
Nine	Three
Ten	Four
Eleven	Three
Twelve	Two
Thirteen	Four
Fourteen	Four
Fifteen	Four
Sixteen	Four
Seventeen	Four
Eighteen	Five
Nineteen	Five
Twenty	Five
Twenty-one	Four
Twenty-two	Four

Table 3 shows median total scores among certain selected subgroups of respondents. The median score was higher among Nepalese students compared to other nationalities. Surprisingly, students whose mother's occupation was a doctor had lower scores. Scholarship students had higher scores compared to self-financing ones.

Table 3: Median total scores among selected subgroups of respondents

Characteristic	Median total score	P value
Nationality		0.000
Nepalese	81	
Indian	75.5	
Sri Lankan	73	
Others	77	
Occupation of mother		0.018
Doctor	71	
Others	78.5	
Housewife	78	
Method of selection	82.5	0.000
Govt. selected	76	
Self-financing		

The free text comments stressed the importance of safe sex in controlling HIV/AIDS. Sex education in schools was felt to be important in controlling the epidemic. The respondents were happy that this important issue was being studied by the investigators.

DISCUSSION

The overall knowledge of the medical students surveyed was good. Certain lacunae were observed and the knowledge and perception among certain subgroups of students was low.

Knowledge about HIV/AIDS is important among medical students because of its increasing prevalence. Medical students should be able to protect themselves against HIV infection during practice. Their perception is important as medical students should be able to provide treatment to AIDS patients. They also have an important role in educating the public about HIV/AIDS. A previous study done in 1999 had revealed AIDS phobia among medical students and the authors had suggested that medical educators help students overcome the phobia.[2] Studies have been carried out among the general population, non-medical and medical students in various countries. A study was carried out on knowledge and beliefs about HIV/AIDS among young people in urban Nepal.[7] The

authors concluded that knowledge of the disease was very high. Married people and females had lesser knowledge than others. Knowledge, attitude and practice regarding HIV/AIDS was studied among the general population in Dakshina Kannada district of Karnataka, India.[8] Significant gaps in knowledge were noted. Male gender, higher education, currently married and reading newspapers were associated with higher scores.

Chinese students were surveyed using a questionnaire for knowledge of and attitudes about HIV/AIDS.[9] Students obtained information about HIV/AIDS from a variety of sources and had a moderate level of knowledge about the condition. Medical students had better knowledge and attitudes than others. Educational programs about sex and sexually transmitted diseases were recommended with medical students playing an important role.[9] A recent study had found that the knowledge, attitude and practice (KAP) of university students about HIV/AIDS was impressive.[4] The authors had recommended voluntary counseling and testing (VCT) services. Misconceptions like HIV is transmitted by sharing of food were also prevalent. A study was carried out to determine the level of awareness of medical students regarding HIV/AIDS, hepatitis B and C.[10] Various misconceptions were noted and the authors concluded that there is a lack of awareness among medical students. Universal precautions should be emphasized.

In the present study the students were under the misconception that HIV/AIDS is a more dangerous disease than hepatitis B. The respondents were equivocal about admitting their or their family's children in a school which admits HIV positive children. This correlates with the finding in a study in Pakistan where over half the respondents felt that HIV-positive students should be excluded from government schools.[11] Over 30% would avoid someone with HIV/AIDS. Students agreed with the statement that homosexuality is a crime. This may reflect the conservative nature of South Asian society where alternative sexual preferences are not accepted. In a study in England, students felt that patients with HIV infection were themselves to blame, some did not deserve treatment and homosexuality could not be accepted as part of a normal lifestyle. [12]Students totally agreed with the statement about coinfection with HIV and TB leading to more severe forms of the two disease, about wider availability of condoms and sex education in schools. A survey carried out in India among new medical students had shown good knowledge and few misconceptions about HIV/AIDS.[13]

In Zagreb, Croatia attitudes towards HIV/AIDS was studied among fourth year medical students during 2002/03 and compared with those to a previously reported one among 1993/4 students.[14] The 2002/03 students had a higher core. Less homophobia, better knowledge about transmission and experience with HIV/AIDS patients were associated with a better attitude. In the present study Nepalese students, students who did not have doctor parents and government selected scholarship students had higher scores. All the scholarship students are Nepalese and the Nepalese self-financing students are selected through an entrance examination conducted by Kathmandu University. Nepalese students perform better academically compared to students of other nationalities. The finding that students with either parent a doctor has lower scores is surprising and difficult to explain. Differences in knowledge and attitude were noted in previous studies. In the British study, Cambridge students had better knowledge about HIV/AIDS than their London counterparts.[12] The Cambridge students however, had a more negative attitude. Differences were noted among subgroups of pharmacy students in a survey in Malaysia.[1] In Pakistan, older students and clinical students were more knowledgeable compared to others.[11] In MCOMS, there was no difference in the knowledge and perception score among preclinical and clinical students.

Certain lacunae in knowledge and perception were noted. Foreign students and self-financing students had lower scores. Educational interventions can be recommended to correct the lacunae. In Nigeria, systematized HIV/AIDS education for student nurses resulted in favorable changes in knowledge and attitude.[15] They were more likely to comply with universal precautions. In Iran, an educational course significantly improved the knowledge and attitude of students towards HIV/AIDS.[16] A Mexican study had looked at teaching of HIV/AIDS in a sample of medical schools. Only 20% of the curricula included teaching of the subject, an average of 8.8 hours only was assigned to its teaching and over 90% of professors involved in teaching had no clinical experience in the field.[17] In MCOMS, though the subject is covered during various semesters of study, the teaching is largely theoretical. Social aspects like telling a patient that he/she is HIV-positive, the social aspects of the disease and preventive health education are not emphasized. Studies among other semesters are needed to find out whether there continues to be lacunae in knowledge among foreign and self-financing students.

The study had limitations. The questionnaire was pretested among three students from other semesters for readability and comprehensibility. Detailed pretesting was not carried out. The practice of students regarding HIV/AIDS was not studied. Only certain selected aspects of the topic were covered in the questionnaire. The response rate especially of the sixth semester students was low. The study was carried out only among certain semesters of students in a single medical school in Nepal. These factors may affect the generalizability and representativeness of the study. This study can be considered as a preliminary one and the authors are considering conducting a much stronger representative study using an improved questionnaire among different semesters of medical students in more number of Nepalese medical schools.

CONCLUSIONS

The overall scores were high but certain misconceptions were noted. The misconceptions should be corrected through education. The scores among foreign and self-financing students were lower compared to the Nepalese. These students may need more education and training on the subject. Studies among other semesters of students and in other Nepalese medical schools should be carried out.

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Appendix: Questionnaire used for the study

Perception and Knowledge regarding HIV/AIDS among students in a medical college in Western Nepal

Semester of study: Nationality: Gender:

Occupation of father: Occupation of mother:

Govt. selected/Self-financing: Urban/Rural

For the following statements score using the following key (1 = strongly disagree with the statement, 2= disagree with the statement, 3= neutral, 4= agree with the statement, 5= strongly agrees with the statement.) Use whole numbers only.

1 HIV/AIDS is a major health and social problem and has the potential to derail the rapid economic growth being achieved.
2 Drugs are available which can cure HIV/AIDS.
3 AIDS is exclusively a disease of homosexuals and cannot affect t heterosexuals.
4 In terms of infectivity, HIV/AIDS is a more dangerous disease than hepatitis B.
5 In my future career, I will be comfortable treating AIDS patients.
6 The basic genetic material of the virus causing HIV is deoxyribonucleic acid.
7 Oral contraceptives can prevent the transmission of HIV.
8 Sharing eating utensils with a HIV positive patient can lead to transmission of the disease.
9 HAART is effective in treating HIV/AIDS.
10 Barber shops and beauty parlors can serve as an important means of spread of HIV.
11 I and my immediate family have no problems enrolling our children in a school which admits HIV positive children.
12 Homosexuality is a crime against God and humanity.
13 Using a condom during sexual intercourse is a reliable protection against HIV/AIDS.
14 Antiretroviral drugs have a high risk of drug interactions.
15 Patent issues and cost are important factors hindering access to newer antiretrovirals.
16 I am comfortable being friends with a HIV positive person.
17 A HIV positive person can safely donate blood.
18 Co infection with HIV and TB can lead to more severe manifestation of both diseases.
19 Condoms should be widely available and condom vending machines should be installed in public places.
20 Sex education in schools can reduce the transmission of HIV.
21 CD4 count is of prognostic importance in HIV infection.
22 Directly observed treatment can be useful in improving compliance in HIV infection.

Any other comments (Please use the back of the sheet) :

Thank You for participating. It is very much appreciated.

THE STUDY OF DRUG INDUCED HEPATOTOXICITY IN ATT PATIENTS ATTENDING IN NATIONAL TUBERCULOSIS CENTER IN BHAKTAPUR

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ABSTRACT

The drug-induced hepatotoxicity is a significantly increasing problem worldwide, but it is of more concern in the treatment of tuberculosis (TB) infection, especially in a third world country like Nepal, where tuberculosis is still endemic. Liver has a central role in drug metabolism and detoxification, and is consequently vulnerable to toxic effects of the drugs. The study was carried out from August 2006 to May 2007. The ATT patients, who visited the chest clinic, were sent to the laboratory for analysis of Liver enzymes (ALT, AST) and bilirubin level. During the period of August 2006 to May 2007 total of 114 patients; 114 blood samples were collected for liver enzymes analysis. It was found that among114 ATT patients; 41 patients (35.0%) had abnormal parameters with the elevation of serum bilirubin level, AST level and ALT level. It showed that drug induced hepatotoxicity due to anti TB drugs is relatively higher rate among lower socio-economic status group. Out of 114 cases, the marked elevation of total bilirubin level (>5.0mg/dl) was found in 15 (13.0%) and mild elevation of bilirubin level (1.1-5.0mg/dl) was found in 25 (22.0%) patients while 74 (65.0%) patients were found to have normal level of bilirubin. Similarly, 17 (15.0%) patients were found to have moderate elevation of ALT level (above 51.0IU/L), 5 (4.0%) patients were found to have slight elevation of ALT level (36-50IU/L) and 92(81.0%) patients had normal level. Likewise 10 (9.0%) patients were found to have moderate elevation of AST level (above 51.0IU/L); 8 (7.0%) had slight elevation of AST level (41-50 IU/L); and 96 (84.0%) were found to have normal level. The facts associated behind these findings are probably poverty, malnourishment, alcohol consumption, illiteracy of people and poor health management system. Hence, for the treatment of TB , with ATT regimens, a baseline laboratory testing and monitoring system should be adopted before starting treatment which might help to reduce drug induced hepatotoxicity in ATT patients.

Keyword : ATT patient, Rifampicin, Ethambutol, Hepatotoxicity, AST, ALT, Enzymes.

INTRODUCTION

Tuberculosis is one of the major causes of morbidity and mortality here in Nepal and most other poor countries and so is the drugs related

hepatotoxicity associated with the treatment of tuberculosis. Liver has a central role in drug metabolism and detoxification, and is consequently vulnerable to the toxic effects of the drugs. The pathogenesis and types of hepatotoxicity are presented, ranging from hepatic adaptation to hepatocellular injury. However the knowledge of the metabolism of anti-TB medications and of the mechanisms involved in hepatotoxicity by ATT is still incomplete.

Structure and function of Liver: The liver is situated between the alimentary tract and the systemic circulation to maximize processing of absorbed nutrients and to minimize exposure of the body to concentration of exogenous substances and their metabolites.

Hepatic Drug Metabolism Transporters, Enzymes, and Excretion: The splanchnic circulation carries ingested

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drugs directly into the liver, a phenomenon known as the "first pass" through the liver. Metabolic enzymes convert these chemicals through phase 1 pathways of oxidation, reduction, or hydrolysis, which are carried out principally by the cytochrome p450 class of enzymes. Phase 2 pathways include glucuronidation, sulfation, acetylation, and glutathione conjugation to form compounds that are readily excreted from the body. Other subsequent steps include deacetylation and deamination. Many drugs may be metabolized through alternative pathways. In phase 3 pathways, cellular transporter proteins facilitate excretion of these compounds into bile or the systemic circulation. Transporter and enzymes activities are influenced by endogenous factors such as circadian rhythms, hormones cytokines, disease states, genetic factors, sex, age, ethnicity and nutritional status, as well as by exogenous drugs or chemicals.[1]

Pathogenesis of drug-induced hepatotoxicity: This may be result from direct toxicity of the primary compound, a metabolite, or from an immunologically mediated response, affecting hepatocytes, billiary epithelial cells, and or liver vasculature. In many cases, exact mechanism and factors contributing to liver toxicity remain poorly understood. Predictable drug induced hepatotoxicity is generally characterized by certain dose – related injury in experimental animal models, has a higher attack rate, and tend to occur rapidly. Injurious free radicals cause hepatocyte necrosis in zones farthest from the hepatic arterioles, where metabolism is greatest and oxidant detoxifying capacity is the least.

Unpredictable reactions comprise most types of drug induced hepatotoxicity. These hypersensitivity or metabolic reactions occur largely independent of dose and relatively rarely for each drug, and may result in hepatocellular injury and or cholestasis. Hepatocyte necrosis is often distributed throughout hepatic lobules rather than being zonal, as is often seen with predictable drug-induced hepatotoxicity.[2.] In hypersensitivity reactions, immunogenic drug or its metabolites may be free or covalently bound to hepatic proteins, forming haptens or neoantigens. Antibody dependent cytotoxic, T-cell, and occasionally eosinophilic hypersensitivity responses may be evoked. Released tumor necrosis factor-alpha, interleukin (IL)-12, and IFN-gamma promote hepatocellular programmed cell death (apoptosis), an effect opposed by IL-4, IL-10, IL-13, and monocyte chemo tactic protein-1.

Metabolic idiosyncratic reactions may result from genetic or acquired variation in drug biotransformation pathways, with synthesis or abnormally slow detoxification of a hepatotoxic metabolite.

Drug-induced hepatotoxicity may occur with all currently recommended regimens for the treatment of tuberculosis infection including isoniazid, rifampicin, pyrazinamide and ethambutol. Among four drugs, isoniazid rifampicin pyrazinamide play major role to cause hepatotoxicity.

Mechanism of liver toxicity

By isoniazid : Normally isoniazid is cleared mostly by the liver, primarily by acetylation by N-acetyl transferase2 (NAT-2). Acetyl-isoniazid is metabolized mainly to mono-acetyl hydrazine (MAH) and to the no toxic diacetyl hydrazine, as well as other minor metabolites. The reactive metabolites of monoacetyl hydrazine (MAH) are probably toxic to tissues through free radical generation. The additional isoniazid metabolites acetyl hydrazine covalently binds to liver macromolecules, a process mediated by microsomal enzyme.[3]

By Rifampicin : Rifampicin may occasionally cause dose dependent interference with bilirubin uptake resulting in sub-clinical, unconjugated hyperbilirubinemia or jaundice without hepatocellular damage. Conjugated hyperbilirubinemia probably is caused by rifampicin inhibiting the major bile salt exporter pump.[4] Asymptomatic elevated bilirubin may also result from dose-depended competition with bilirubin for clearance at sinusoidal membrane or from impeded secretion at the canalicular level.[5]

By Pyrazinamide : It may exhibit both dose dependent and idiosyncratic hepatotoxicity. Pyrazinamide alters nicotinamide acetyl dehydrogenase levels in liver[6] which might result in generation of free radical species. There may be shared mechanisms of injury for isoniazid and pyrizinamide, because there is some similarity in molecular structure. Patients who previously had hepatotoxic reactions with isoniazid have more severe reaction with rifampicin and pyrazinamide.

By Ethambutol : There has been one report of ethambutol related liver cholestatic jaundice with unclear circumstances.

METHODOLOGY

The ATT patients who come to NTC from different DOTS clinics for follow-up visit and monitoring of the DOTS

treatment were taken into the study. The study was carried out from August 2006 to May 2007. The ATT patients visited to the chest clinic were sent to the laboratory for analysis of Liver enzymes (ALT, AST) and bilirubin level. During the period of August 2006 to May 2007, total of 114 patients were received from the OPD clinic for Liver enzymes analysis in the clinical lab. Blood samples were collected from the patients and serum was separated. The liver enzymes Alanine transaminase (ALT), Aspartate transaminase (AST) and Bilirubin analysis were done. The ALT and AST were analyzed by kinetic method using semi auto analyzer and bilirubin was analyzed by color end point method using semi autoanalyser. The control sample was also used for monitoring each steps of procedure and analyzer machine.

RESULT

Out of 114 patients, 62 were male and 52 were female. Among the age group, 18(15.7%) were under 20 yrs, 61(53.5%) were 21-40yrs, 31(27.1%) were 41-60year of age and 4(3.5%) were above 60year age.

Table 1: Age and sex group of ATT patients

Age groups (yrs)	Sex		Total	Percentage
	Male	Female		
<20	9	9	18	15.7%
21-40	32	29	61	53.5%
41-60	18	13	31	27.1%
>60	3	1	4	3.5%
Total	**62**	**52**	**114**	**100.0%**

Out of total 114 patients, 41(35%) showed abnormal pattern of liver function, i.e. elevation of serum bilirubin, serum alinine transaminase (ALT) and serum aspartate transaminase (AST). 73(65%) showed normal pattern of the liver function; i.e. normal level of S. bilirubin, alanine transaminase (ALT), aspartate transaminase (AST).

Table 2: Pattern of liver function

Age group	Normal pattern	Abnormal pattern	Total
0-20	11(61.1%)	7(38.8%)	18(100.0%)
21-40	42(68.9%)	19(31.1%)	61(100.0%)
41-60	17(54.9%)	14(45.1%)	31(100.0%)
>60	3(75.0%)	1(25.0%)	4(100.0%)
Total	**73(65%)**	**41(35%)**	**114(100%)**

Out of 114 ATT patients, the bilirubin level was found to be greater than 5.0mg/dl in 15(13.0%) patients; bilirubin level of 1.5-5.0mg/dl was found in 25(22.0%) patients and 74(65.0% %) patients had normal bilirubin level. Similarly, 17(15.0%) patients had moderate elevation of ALT level (>51.0 IU/L); 5(4.0 %) patients had slight elevation of ALT level ranging from 36-50 IU/L and 92 (81.0%) patients were found to have their ALT level within the normal range.

Meanwhile, 10 (9.0%) patients turned out to have moderate elevation of AST level (>51.0 IU/L) and 8(7.0%) were found to have slight elevation of AST level ranging from 41.0-50.0 IU/L; and 96 (84.%) patients had their AST level within normal range.

Table 3: Result of bilirubin parameters

Range of Bilirubin level, mg/dl	No. of patients	Percentage
0.1-1.0 (normal range)	74	65.0%
1.1-5.0 (mild increase)	25	22.0%
>5.0 (moderate increase)	15	13.0%
Total	**114**	**100.0%**

Table 4: ALT parameter

Range of ALT (IU/L)	No. of patients	Percentage
<35.0 (normal range)	92	81.0%
36.0-50.0 (mild increase)	5	4.0%
>51.0 (moderate increase)	17	15.0%
Total	**114**	**100.0%**

Table 5: AST parameter

Range of AST (IU/L)	No. of patients	Percentage
<40.0 (Normal range)	96	84.0%
41.0-50.0 (mild increase)	8	7.0%
>51.0 (moderate increase)	10	9.0%
Total	**114**	**100.0%**

DISCUSSION

As per the results, it was found that among 114 ATT patients 41 (35.0%) had abnormal parameters with the elevation of

serum bilirubin level, AST level and ALT level. It showed that drug induced hepatotoxicity due to anti TB drugs is relatively higher among the low income status compared to general literature and data's suggestion.[7]. The probable causes behind these findings could be poor nutrition, alcohol consumption, HIV co-infection many more. Each factor should be taken into account before definitive conclusions can be drawn, however it is beyond the scope of this study to establish cause and affect relationship with various above mentioned factors. Several studies suggested that increasing age is a risk factor for TB drugs induced hepatotoxicity but statistical significant was not achieved. One study reported hepatotoxicity rate ranging from 2.0 to 8.0% as age increased, with an average[8] of 5.0%. Other studies have reported that hepatotoxicity ranges from 22.0 to 33.0% in those older than 35 years. Out of 114 cases, age group ranging from 41-60 yrs had the greatest prevalence (45%)of abnormal liver function parameters, while the rates of abnormal liver parameters in age group <20 and 20-40 yrs. were similar and the age group >60 yrs. contributed least to the percentage of the patient with abnormal liver parameters, namely elevated AST, ALT and Bilirubin. Out of 114 patients, almost 35% of patient had abnormal bilirubin level with 13% out of the total patients having marked elevation of bilirubin. Meanwhile more than 80% of the patients had normal level of AST and ALT level and only 15% and 10% had markedly elevated AST and ALT level respectively. At the same time, related literature shows overall risk of hepatotoxicity ranges from 5%-33% in those undergoing TB treatment, with rate increasing as the age of patients under treatment increases.[9] Similarly, it is shown in other study that in children younger than 5 yrs , with extra pulmonary TB including TB meningitis treated with Isoniazid , Rifampicin and Pyrazinamide, more than 82% had ALT of more than 100 IU/L and more than 40% developed asymptomatic hepatitis.[10] Several studies also reported increased risk of hepatotoxicity in women especially pregnant one.[11,12] Likewise in alcohol user, several studies have indicated that alcohol use also induce the hepatotoxicity in ATT patients.[13,14] Other associated factors include malnutrition or hypoalbuminemia, HIV infection, Hepatitis B infection, Hepatitis C infection and second line ATT drugs conditions. Although in Nepal, there is hardly 2.5% of TB- HIV co-infection reported and association of TB and Hepatitis B and C infection and HIV infection has not been studied and reported in Nepal, their importance and significance can't be over emphasized.

CONCLUSION

Overall, drug induced hepatotoxicity in ATT patient was found to be higher than 34%, however, the age , sex , disease conditions, nutrition status, alcohol abuse and other possible confounding factors play statistically significant role. The reasons behind this higher level of drug induced hepatotoxicity are probably poverty, malnourishment, alcohol consumption, illiteracy of people and poor health management system with age playing a significant role. For better cause and effect relationship with less bias and for clinical significance, a broader, controlled cohort study of larger size is recommended. For now, with an effective DOTS program accessible all over the country, a baseline laboratory testing criteria and monitoring system should be adopted before starting treatment to effectively reduce the treatment related morbidities.[15]. Along with this patient and staff education, appropriate selection of patients for treatment, careful regimen selection and monitoring will minimize the associated risk and adverse effects. The ability to adapt to changing medical landscape will be crucial to continue safe and effective treatment of TB.

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COMPARISON OF BRONCHODILATOR EFFECT OF SALBUTAMOL DELIVERED VIA MDI AND DPI IN COPD PATIENTS

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ABSTRACT

Introduction : Chronic Obstructive Pulmonary Disease (COPD) is one of the leading problems affecting majority of population all over the world which diminishes the quality of life of the individual and create extra burden to the society as well as country. Inhaled bronchodilator therapy is the mainstay of treatment in the management of COPD. Various inhaled [e.g. metered dose inhaler (MDI) /dry powder inhaler (DPI)] formulations are available and are widely used among the COPD patients in Nepal.

Methodology : This is cross sectional prospective study, designed to compare the bronchodilating effect produced when salbutamol is delivered via two devices: MDI (Asthalin® from Cipla) and DPI (Asthalin® rotacap delivered via Rotahaler® from Cipla), in patients with stable COPD. It is proven by previous studies that intervention is necessary to improve the compliance of the patients; all subjects (total n=60; 30 in each group) are counseled and trained to follow correct inhaling technique through particular device. Then their improvements in lung function were measured with reference to the pulmonary function test based on spirometry.

Results : Patients enrolled in each group were not statistically different regarding to age (P=0.318), weight (P=0.324) & BMI (P=0.836). Among the total subjects 87% had smoking history and 2% were still smoking and there was no significant difference in smoking habit between the two groups (p-value 0.544 > 0.05). Similarly 91.6 % of the total had exposure to indoor air pollution which had been the major risk factor for COPD. Most of the patients were on stage II COPD (62%). Salbutamol was found to have no effect on vital statistics of patients. Study showed there was no significant difference in the improvement of forced expiratory volume in one second (FEV1) (p=0.802), FVC (p= 0.693), FEV1 % (p=1) and PEF (p=0.448) between MDI and Rotahaler groups. Major side effect associated with the MDI users is headache (79%) while those among Rotahaler users were muscle cramps (79%). Even though intervention improved the inhaler using technique among the patients in both the groups, it was found even after counseling, DPI seemed to be better understood by the patients in comparison to MDI (p=0.003 & 0.00). In addition DPI was preferred by most of the patients who were familiar with both delivery systems. It was also found to be cheaper than the MDI.

Conclusion : Overall evidence suggests that although both MDI & DPI improve the lung function of COPD patients to similar extent, DPI is cheaper and more preferred and can be easily handled by the patients which can result in reduction of non-compliance.

Keyword : COPD. Salbutamol, DPI, MDI, Spirometry

INTRODUCTION

COPD stands for Chronic Obstructive Pulmonary Disease.[1] Chronic obstructive pulmonary disease is a lung ailment that is characterized by a persistent blockage of airflow from the lungs which is an under-diagnosed, life-threatening lung disease that interferes with normal breathing and is not fully reversible.[2] COPD is not one single disease but an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow; the more familiar terms are 'chronic bronchitis' and 'emphysema'.[3]

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According to the latest WHO estimates (2007), currently 210 million people have COPD and 3 million people died of COPD in 2005. WHO predicts that COPD will become the third leading cause of death worldwide by 2030.[3]

In Nepal, a combination of asthma and bronchitis constitutes a major cause of mortality.[4] It is estimated that about 7500 people, most of whom are children, lose their lives each year in Nepal due to indoor air pollution (IAP) related Acute Lower Respiratory Infections (ALRI) and COPD.[5]

COPD can not be cured, but it can be controlled.[1] Prevention of disease progression, improvement of symptoms, exercise tolerance and health status and decrease in exacerbations and mortality are the goals of management.[6]

The inhaled route is preferred in the therapy of COPD as small doses of drugs are delivered direct to their site of action, leading to a rapid onset of action and a low incidence of side effects.[7] The airways are treated but less drug reach to the other parts of the body.[8] Inhaled medications are intended to exert localized, site-specific therapeutic effects on the bronchioles.[9] Thus inhaled bronchodilator therapy is the mainstay of treatment in the management of COPD. Inhaled short acting bronchodilator is recommended for symptoms in mild disease, whereas inhaled long acting bronchodilator is recommended for maintenance therapy of daily symptoms.[6]

The effectiveness of inhaled bronchodilator in individual patients is assessed by comparing measurements from pulmonary function tests made before and after administration of the drugs.[10,11] Generally, forced expiratory volume in one second (FEV1) is the marker used, in line with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[12,13]

Various inhaled formulations [metered dose inhaler (MDI) / dry powder inhaler (DPI) or Nebulizer] are available but it is the MDI, which is most commonly prescribed.[14] Although nebulizers are frequently used to deliver COPD treatment, particularly to less mobile patients, most current designs are bulky and inconvenient, and treatment times are longer. Therefore, they are better categorized as fallback devices for most COPD patients. They are not true competitors to pressurized metered-dose inhalers (pMDIs) and DPIs for outpatient use.[15]

There is no perfect inhaler, and each has advantages and disadvantages, but there is increasing recognition that a successful clinical outcome is determined as much by choice of an appropriate inhaler device as by the drugs that go in them.[16] Drug delivery from all inhaler devices depends on how the patient prepares the device and then inhales from it. The best device for COPD patients is arguably one for which both these steps can be performed successfully without major challenges.

There is evidence that a patient is most likely to use correctly an inhaler that he or she prefers.[17] Choice of an inhaler device should therefore take into account the likelihood that patients will be able to use a particular device correctly, cost-effectiveness, preference and likely compliance.

This is significantly important to compare the cost and benefit between MDI and DPI for patient with COPD to achieve the definite therapeutic outcome. Hence the study is mostly focused on to analyze the device preference of the patients and their capability of producing improvement in pulmonary function.

METHODS

Study Design

This was cross sectional prospective study.

Study Site and duration

The study was conducted in Dhulikhel Hospital, Kathmandu University Teaching Hospital, Dhulikhel from Dec 2007 to June 2008.

Sample selection criteria

Patients from out patient department as well as from in patient department who had age above 15 years with the documented diagnosis of COPD and prescribed with salbutamol inhaler (200 µg dose) were included in the sample. However patients with following criteria were excluded in the sample.

- Unstable angina
- Recent pneumothorax
- Recent heart attack or stroke
- Recent eye or abdominal surgery
- Coughed up blood recently and the cause is notknown
- Patient prescribed with corticosteroids

Sample size

Sixty (n=60) consecutive patients who fulfilled the inclusion criteria were included in the study. All patients were then further divided into MDI and DPI groups (thirty in each group) according to the type of salbutamol inhaler they were prescribed with as well as on their own preference if they were familiar with both inhalers.

Each patient of MDI group (n=30) received 200 µg (two puffs in one minute interval) salbutamol four times a day via a MDI (ASTHALIN CFC free inhaler, Manufactured by CIPLA, Ltd. INDIA containing 200 Metered dose and each puff containing 100 µg of Salbutamol) as per MDI score technique .While patients of DPI group (n=30) received 200 µg of salbutamol via Rotahaler (ASTHALIN Rotacap, Manufactured by CIPLA, Ltd. INDIA; each Rotacap containing 200 µg of Salbutamol for use with Rotahaler) four times a day as per DPI scores technique.

Data Collection

At first, patients who met the inclusion criterias, were told about the study being done and about their contribution in this study. After taking informed consent from the patients, they were directly interviewed using structured questionnaire. The key data information included age, sex, literacy, occupation, races, smoking/ alcohol habit and exposure to any air outdoor or indoor air pollution. Additional information about date of diagnosis of COPD, drug treatment for COPD and other concomitant diseases and abnormal clinical findings were recorded from medical case record.

Patients were counseled about how to use the inhaler they were prescribed with, for those who were using inhaler for the first time. For those who were already using inhaler, knowledge about using technique of particular inhaler (MDI or DPI) was checked. If they did wrong they were counseled and demonstrated (using device without active ingredient) how to use it correctly. The improvement in inhaler using technique was evaluated by scoring each correct step using Rotahaler/ Meter Dose Inhaler Technique Score Chart just after counseling and also on follow up.

After counseling, spirometric test was performed in each patient by using the spirometer (Vitalograph) to find out the baseline lung functions. If the patient was already using the salbutamol inhaler, after consultation with the physician, the patient was made to escape the dose of the medicines 6 hrs before the spirometry evaluation to get the baseline results.

During the spirometric test each patient was asked to take the deepest breath he/she could, and then to exhale into the sensor as forcefully as possible and for as long as possible. During the test, soft nose clip was used to prevent air escaping through the nose. The present lung functions of the patients were displayed in terms of FVC (Forced Vital Capacity) (Liters), FEV1 (Liters) and PEF (Liters/ second). Standard values for each patient differ according to their height, age, sex, and sometimes race and weight. After the baseline evaluation, the usual dose i.e. 200 µg of salbutamol was given to the patients at the same time his/her inhalation technique was also checked and then spirometric analysis was repeated as follow up to find out the improvement in lung function.

The blood pressure (BP), respiration rate (RR), pulse rate (PR) and potassium level were also assessed before and after the use of bronchodilator to find out if there was any change. The spirometric test, vital statistics (BP, RR, PR), potassium level, understanding of inhalation technique, health problems they faced during therapy were again investigated in follow up visit after two weeks (usually 14-20 days) of each patients of both groups.

Data analysis

The data collected by using structured questionnaire and reviewing medical record forms were entered into a computer file and were expressed into codes for the purpose of analysis. The data with qualitative variables were summarized and expressed as frequency and percentage. The data with quantitative variables were expressed as mean and standard deviation (SD) and were analyzed by using statistical tests.

Patient's age, weight, height and BMI were compared using Mann-Whitney U test. Change in Vital Statistics (BP, RR, PR), potassium level and improvement in lung function parameters (FVC, FEV1, FEV1%, PEF) after using salbutamol via particular inhaler (MDI or DPI) were analyzed by Wilcoxon Signed Ranks Test. While comparison of same variables including oxygen saturation between two different groups was carried out by using Mann-Whitney U test. MDI and DPI scores were compared for the values before counseling, after 30 min of bronchodilator and after two weeks of starting bronchodilator by using Mann-Whitney U

test. All data were analyzed at the 5% significance level. The data were significant for p<0.05. All analysis was done by using statistical software SPSS 15 and graphs were plotted in Excel 2003 and 2007.

RESULTS

Table 1: Demographic Characteristics

Variables	Characteristics	MDI (n=30)	DPI (n=30)	p-value
Age, years (Mean ± SD)		61.20 ± 13.52	59.00 ± 11.03	0.318
Age group, years	<40	1	1	
	40-49	3	4	
	50-59	9	10	
	60-69	6	9	
	70-79	10	5	
	>=80	1	1	
Gender	Female	28	23	
	Male	2	7	
Ethnic Group	Magar	5	4	
	Newar	8	11	
	Chettri	6	3	
	Brahmin	8	9	
	Others+	3	3	
Education	Literate	2	6	
	Illiterate	28	24	
Employment	Farmer	17	22	
	Housewife	11	6	
	Service	1	0	
	Shopkeeper	0	1	
	Other++	1	1	

Others+: Rokka, Giri, Pariyar, Lohala, Shanker, Thokar; Other++: Masson, Student

Table 2: Anthropometric Measurements

Variables	MDI (n=30)	DPI (n=30)	P-value
Weight (Kg)	44.83 ± 9.27	46.57 ± 7.22	0.324
Height (cm)	148.77 ± 6.17	152.6 ± 7.11	0.049
BMI status (kg/ m^2)	20.27 ± 3.97	19.77 ± 2.81	0.836
Under weight (BMI <18.5)	11	10	
Normal weight(BMI 18.5-24.9)	16	18	
Overweight(BMI 25-29.9)	1	2	
Obese(BMI ≥ 30)	2	0	

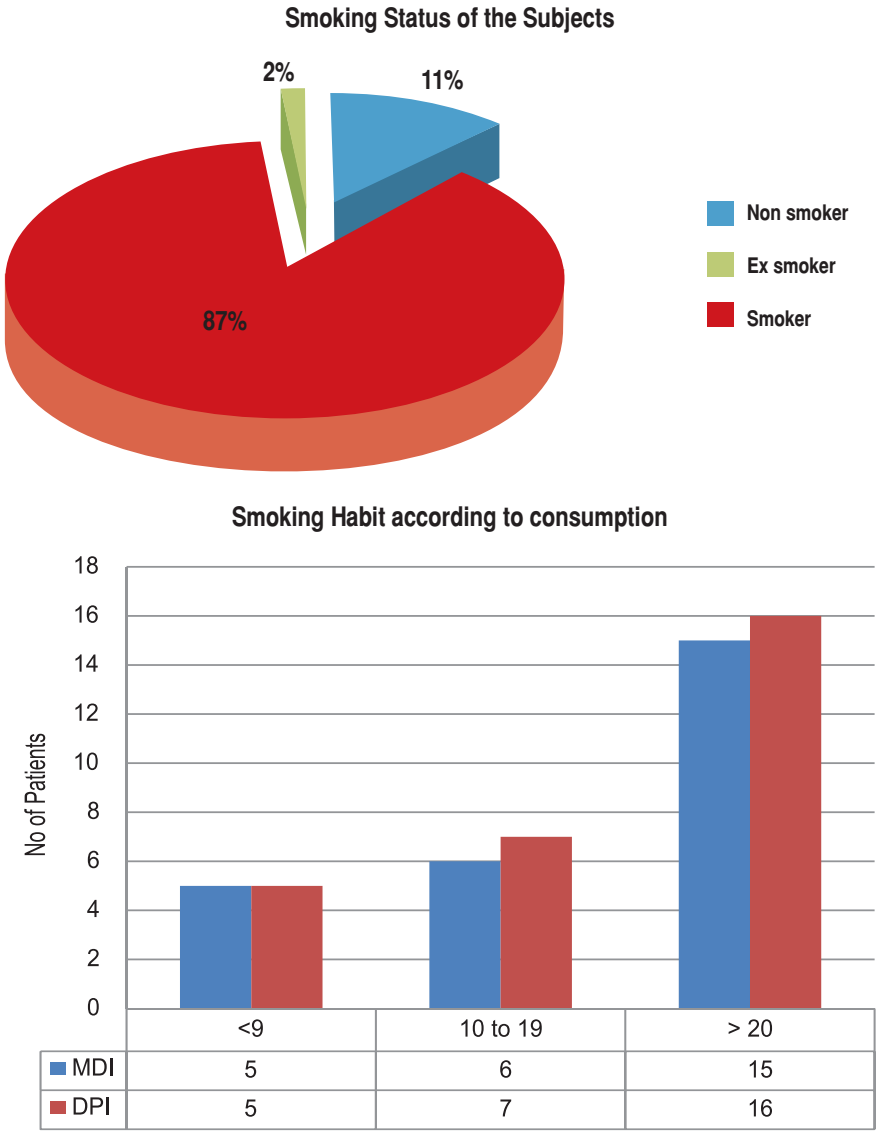

Figure 1: Smoking habit

Study of vital statistics of the participants

Table 3: Comparison of vital statistics and oxygen saturation of the participants between two groups i.e. MDI & DPI (Mann-Whitney U)

Measures	MDI - P-values	DPI - P-values
Δ SBP (after 30 mins) from baseline	0.227	0.414
Δ SBP (after two weeks) from baseline	0.068	0.157
Δ DBP (after 30 mins) from baseline	0.234	0.107
Δ DBP (after two weeks) from baseline	0.36	0.19
Δ RR (after 30 mins) from baseline	0.395	0.011
Δ RR (after two weeks) from baseline	0.011	0.039
Change in mean value of PR	MDI	DPI

Before medication	89.2 ± 14.97	86.23 ± 12.86
After 30 mins	87.87 ± 14.19	85.57 ± 0.58
After two weeks	83.2 ± 8.67	82.6 ± 8.39

Δ = change from baseline after bronchodilator therapy, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, RR = Respiration rate, PR = Pulse rate

Table 4: Spiro-metric analysis

4.1 Analysis of bronchodilating effect of salbutamol within each group (Wilcoxon Rank Test)		
	MDI	DPI
STD FVC	2.14 ± 0.51	2.56 ± 0.52
Baseline FVC	0.92 ± 0.72	0.96 ± 0.47
FVC after 30 mins of bronchodilator	1.16 ± .80	1.18 ± 0.52
FVC after 2 weeks of bronchodilator	1.23 ± 0.65	1.26 ± 0.45
p- value (FVC after30-FVC baseline)	0	0
p- value (FVC after two weeks-FVC baseline)	0	0
Std FEV1	1.78 ± 0.48	2.12 ± 0.4
Baseline FEV1	0.75 ± 0.67	0.75 ± 0.42
FEV1after 30 mins of bronchodilator	0.91± 0.73	0.88 ± 0.41
FEV1after two weeks of bronchodilator	0.95 ± 0.52	0.97 ± 0.40
p- value (FEV1 after30-FEV1 Baseline)	0	0.002
p- value (FEV1 after two weeks-FEV1 Baseline)	0	0
Std PEF	318.93 ± 42.97	349.97± 45.05
Baseline PEF	117.63 ± 96.65	110 ± 76.33
PEF after 30 mins of bronchodilator	121.63 ± 94.65	116.86± 64.11
PEF after 2 weeks of bronchodilator	134.4 ± 82.61	137.35 ± 84.66
p- value (PEF after 30-PEF baseline)	0.066	0.182
p- value (PEF after two weeks-PEF baseline)	0.016	0

Standard values are based on individuals' age, height and gender and automatically displayed by spirometer.

4.2 Comparison of improvement between two groups (Mann Whitney U Test)			
Measures	MDI Group	DPI Group	p-Value
FEV1			
Baseline	0.75 ± 0.67	0.75 ± 0.42	0.268
Improvement after 30 Mins	0.16 ± 0.18	0.13 ± 0.2	0.295
Improvement after 2 weeks	0.21 ± 0.28	0.22 ± 0.24	0.802
FVC			
Baseline	0.92 ± 0.72	0.96 ± 0.47	0.15

Improvement after 30 Mins	0.24 ± 0.21	0.21 ± 0.23	0.705
Improvement after 2 weeks	0.31 ± 0.21	0.30 ± 0.25	0.693
PEF			
Baseline	117.63 ± 96.6	110 ± 76.33	0.988
Improvement after 30 Mins	4 ± 45.3	6.86 ± 28.4	0.802
Improvement after 2 weeks	16.77 ± 41.8	27.34 ± 33.9	0.448

Improvement after 30 mins = Post- bronchodilator values after 30 mins- Baseline values

Improvement after two weeks = Post- bronchodilator values after two weeks - Baseline values

Inhaler using Technique Score

Table 5: Understanding of the patients how to use the particular inhaler

Measures	MDI Group	DPI Group	p- Value
Placebo Score	4.97 ± 2.10	4.87 ± 1.46	0.478
Score after counseling	8.6 ± 0.81	9.23 ± 0.68	0.003
Score in follow up	8.4 ± 0.67	9.47 ± 0.57	0

Table 6 : Side effects associated with a particular device

Measures	MDI (4)	DPI (7)
K-level	3.33 ± 0.09	3.24 ± 0.17
P- value	0.001	0.004

Table 7: Cost comparison of MDI and DPI

	MDI	DPI
Unit price per item (Nepali Rupees)	148.00	27.00
Cost of device	-	119.00
No of administration per package	100	30
Unit cost per administration	1.48	0.9
Cost of device per dose *		0.02
Total cost per administration	1.48	0.92

*Assuming Rotahaler device will last for 5 years.

DISCUSSION

Among the total Newars made up the highest population (32%) followed by Brahmin (28%). It was found that most of the patients were illiterate in both group, only about 7% in MDI and 20% in DPI were literate. Farmer constitutes the more than half of the population (57%) followed by housewife (37%).

The mean age of COPD patients was 61.20±13.52 for MDI and 59.00±11.03 for DPI group respectively. Both MDI and DPI users included in study have similar age as there is no significant difference (p-value 0.318> 0.05; Mann-Whitney U test).

While analyzing among total no of Patients, most of the patients were having normal weight (57%), while some of them (35%) were categorized under underweight group as their BMI was <18.5 which is the prognostic factor for mortality.

Blood pressure, pulse rate, respiration rate and oxygen saturation were checked and analyzed in all patients before and after the use of bronchodilator within and between two groups. Baseline vital signs of both groups were similar (p-value>0.05). There was no significant difference in baseline BP, PR and RR of the patients between two groups. After bronchodilator use, subjects in both groups showed similar BP, PR and RR. No significant difference between the devices was found in terms of vitals (P > 0.05; Mann Whitney Test).

Both delivery systems i.e. MDI and DPI were found equally capable to produce bronchodilating effect of Salbutamol. All parameters FEV1, FVC and FEV1% were significantly improved from baseline as the mean difference of these values between pre and post bronchodilator (after 30 minutes as well as after two weeks) were found significant, (P-values < 0.05, Wilcoxon rank test; table 5.1).

There were no significant differences between two groups in terms of improvement in FEV1, FVC and PEF level (P > 0.05) after bronchodilator therapy. It proved there is the therapeutic equivalence between two delivery systems i.e. MDI and DPI at 200 µg dose of Salbutamol (table 5.2).

Even though about 87% (52 out of 60) were already using the device to deliver the medicine their knowledge about the correct using technique seemed very low; 4.97 ± 2.10 (MDI) & 4.87 ± 1.46 (Rotahaler) when analyzed in Placebo. Most of them were given wrong instruction about the technique from medical shops outside the hospital (e.g. in some cases of Rotahaler, they were instructed to break the capsule by themselves and then poured into the Rotahaler for inhalation) and others who get correct instruction were also making many crucial mistakes. For example in case of MDI, not holding the device in upright position & not closing the mouth properly so that fumes were seemed escaping from mouth were observed in most of the patients. In both groups (MDI as well as Rotahaler) exhalation before inhalation & holding the breath after inhaling the medicine were missing. Studies also showed that many patients fail to hold inhaled medication in their lungs for the full 10 seconds, this final step in the inhaler technique is required for optimal pulmonary absorption of medication, regardless of type of device used.

Drug cost of unit dosage form for DPI was found to be lesser than that of MDI. The socioeconomic status of Nepalese people is low; particularly in the study area (Dhulikhel). The cost analysis would be helpful in recommending the affordable one between two therapeutically equivalent delivery systems. In this case, Rotahaler a simplest DPI was found to be therapeutically equivalent to MDI and is the cheaper one.

CONCLUSION AND RECOMMENDATION

The bronchodilator response was found to be similar irrespective of drug delivery system.[17] It is possible that the DPI deposited the same amount of drug at the site of action as the MDI in patients with COPD. Intervention on inhaler technique improved the patient knowledge which is very crucial to achieve the definite therapeutic outcome. Though all patients showed similar skill at the initial stage (p=0.478), the final score of inhalation technique was significantly improved in case of DPI (p=0.003; 8.6 ± 0.81 for MDI Vs 9.23 ± 0.68 for DPI). Patients using Salbutamol are prone to suffer from hypokalemia in both patterns of delivery (for MDI 3.33 ± 0.09 mol/l; p-value=0.001 and for DPI 3.24 ± 0.17 mol/l; p-value=0.004).

The cost of treatment with DPI is found to be much lesser than that of MDI. Overall evidences from efficacy and cost analysis it seems that treatment of COPD patients with bronchodilator using DPI is more preferable than MDI even though both have similar clinical efficacy.

RECOMMENDATIONS FOR PRACTICE INCLUDE:

- Intervention is essential to improve inhalation technique.
- Nutrition intervention is essential as most of the patients are with BMI <21 kg/m^2 which is the major cause of morbidity.
- Potassium level should be checked in routine intervals there is a chance of hypokalemia.
- Even though both delivery systems have therapeutic equivalence, patient's choice should be given the first preference to improve the compliance.
- As the previous study as well as this study suggests therapeutic efficacy is dose dependent rather than device further research should be conducted at different doses with wide range at large population from two delivery systems.

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NEPALESE PEOPLE'S KNOWLEDGE ABOUT TUBERCULOSIS

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ABSTRACT

Introduction : Tuberculosis (TB) is a major cause of illness and death worldwide, especially in Asia and Africa.

Objective: Objective of this study was to determine Nepalese people's knowledge about tuberculosis.

Methods : The diagnosed cases of tuberculosis was randomly selected, structured questionnaires were used to collect patient knowledge about tuberculosis.

Results : This prospective study included 300 diagnosed cases of pulmonary tuberculosis who were attending the DOTS programme of Nepal. Tuberculosis was most commonly found in economically active age group (21-50 years old). The incidence of tuberculosis was found higher in male than female. Regarding the common part of the body affected by TB bacilli 58% correctly said that it is the Lungs. About the mode of transmission of tuberculosis 50% knew that it is transmitted by droplet infections. More then two third of the respondents had knowledge about the clinical symptoms of tuberculosis, among them chronic cough (82%), evening rise of temperature (72%) and blood in the sputum (72%) were the major symptoms described. Only 16.6% of the respondents knew that Tuberculosis is an common opportunistic infection in people infected with HIV/AIDS. 53.3% patients responded correctly that body secretion like sputum contains Tubercle Bacilli and regarding disposal of sputum and other body fluids 30% said that incineration is the proper way of disposal. On prevention of spread of tuberculosis 31.6% said that TB patients should use mask.

Conclusion : The study found that majority of the patients had satisfactory knowledge about the signs and symptoms of Tuberculosis but their knowledge about causative agent for Tuberculosis, disposal method for sputum and body fluid and preventive method for tuberculosis was still low. It is recommended that National tuberculosis control authority should design health education programme focusing on causative agents, disposal of sputum and body fluids and prevention of Tuberculosis. The awareness campaign should be targeted to patients, family members, community and health care providers and should be disseminated through the media that will reach the general Public. Such awareness campaign will increase the patient's general awareness about the disease and will help to reduce transmission of disease, prevent drug resistant cases and improve the efficacy of DOTS programme.

Keywords : HIV/AIDS, TB, Mycobacterium tuberculosis

INTRODUCTION

Tuberculosis (TB) is a major cause of illness and death worldwide, especially in Asia and Africa. According to the World Health Organization (WHO), one third of the world's population has been exposed to the tuberculosis pathogen.[1] By the end of 2007, 202 of 212 countries and territories had reported case notifications for 2006 and/or treatment

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outcomes for patients registered in 2005. These countries include 99.6% of the world's population. Surveillance and survey data has estimated that 9.2 million new cases of TB occurred in 2006 (139 per 100, 000), including 4.1 million (62 per 100 000) new smear-positive cases. These numbers also includes TB in HIV-positive people. In terms of incidence, among the top five countries, India ranks first followed by China, Indonesia, South Africa and Nigeria. In 2006, Asia (South-East Asia and Western Pacific regions) accounted for 55% of global cases Africa 31% and other three regions accounted for remaining fraction of cases.[2]

Among the 9.2 million new cases of TB in 2006, it is estimated that around 709 000 (7.7%) were HIV-positive. This estimation is based on the global estimates of HIV prevalence among the general population (all ages) published by the Joint United Nations Programme on HIV/ AIDS (UNAIDS) and WHO in December 2007.[3] Tuberculosis is also the world's greatest infectious killer of women of reproductive age and the leading cause of death among people with HIV/AIDS.[4]

The rise in HIV infections and the neglect of TB control programs have enabled a resurgence of tuberculosis.[5] The emergence of drug-resistant strains has also contributed to this new epidemic. From 2000 to 2004 it is estimated that 20% of TB cases are resistant to standard treatments and 2% resistant to second-line drugs.[6] The incidence of TB varies with age. In Africa, TB primarily affects adolescents and young adults.[7] However, in countries where TB has gone from high to low incidence, such as the United States, TB is mainly a disease of older people, or of the immuno-compromised.[8, 9]

There are a number of known factors that make people more susceptible to TB infection: HIV infection is one of the most important factor for susceptibility to TB infection as in Sub-Sahara African countries where the incidence of HIV is high.[10, 11] Smoking more than 20 cigarettes a day is said to increases the risk of TB by two to four times.[12, 13] Diabetes mellitus is also an important risk factor that is growing in importance in developing countries.[14] Other disease states that increase the risk of developing tuberculosis are Hodgkin lymphoma, end-stage renal disease, chronic lung disease, malnutrition, and alcoholism.[8]

Tuberculosis (TB) still remains one of the major Public Health problems in Nepal. About 45% population is infected with TB, of which 60% are adult. Every year, 40,000 people develop active TB, of whom 20,000 have infectious type of pulmonary TB. Although introduction of DOTS has already reduced the numbers of deaths, however 5,000 to 7,000 people still continue to die each year.[15]

The burden of TB has significantly increased because of increased transmission due to Population migration, armed conflict and refugee movement Tuberculosis is transmitted mainly by droplet infection and droplet nuclei generated by sputum positive patients with pulmonary tuberculosis. To transmit infection, the particles must be fresh enough to carry a viable organism. Coughing generates the largest number of droplets of all sizes. The frequency and vigour of cough and the ventilation of the environment influence transmission of infection. Patients with extra-pulmonary tuberculosis or smear negative tuberculosis constitute a minimal hazard for transmission of infection. Tuberculosis is a social disease with medical aspects. The social factors include many non-medical factors such as poor quality of life, poor housing, and overcrowding, population explosion, under-nutrition, lack of education, large families, early marriages, lack of awareness of causes of illness, etc.[16]

OBJECTIVE

Objective of this study was to determine Nepalese people's knowledge about tuberculosis.

MATERIALS AND METHODS

The present prospective study was carried out among tuberculosis patients attending Directly Observed Treatment Short Course (DOTS) Programme in Kathmandu Medical College, Sinamangal and German Nepal Tuberculosis Project Kathmandu, Nepal, during the period from January 2006 to December 2007. A structured questionnaire prepared in English and translated into Nepali language was the tool for data collection. The research objective and methods were explained to the patients, and verbal consent was obtained from them before data collection. Random Sampling method was used to select the target population for the survey. Open ended self administered questionnaires based on the knowledge about Tuberculosis were given to the survey population, literate group were asked to fill up the questionnaire and illiterate group were interviewed by trained interviewer.

The questionnaire consisted of two sections: Section one had details about the patient's background characteristics (age, sex,). Section two consisted of details about knowledge on Tuberculosis like parts of the body affected by TB bacilli, mode of transmission, clinical symptoms,

relationship of HIV and TB, body secretion where tubercle bacilli are found, and proper disposal of sputum and other body fluids. The questionnaire also contains knowledge of the participant on preventive method of tuberculosis transmission.

Data was analyzed by EPI-Info version 3.3.2, document version 8.08 updated Sept 2005 and presented by means of tables and diagrams.

RESULTS

The majority (73%) of the respondents were in the age group of 21-50 years, with males being more (64%) then

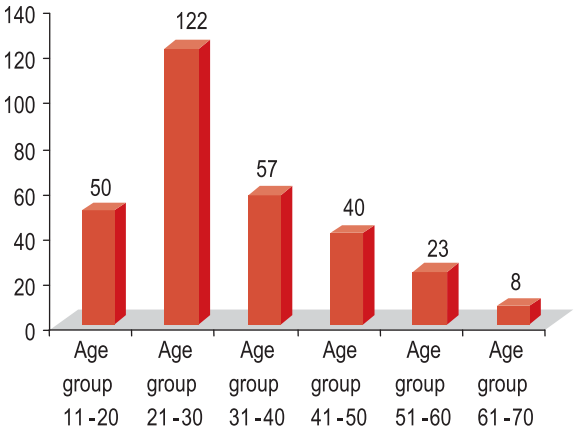

Figure 1: Age wise distribution of patients

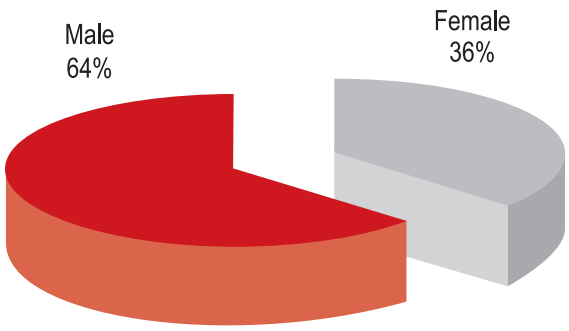

Figure 2: Gender wise distribution of patients

females (36%). Age and sex wise distribution of patients are shown in figure 1 and 2 respectively.

Knowledge on the parts of the body affected by TB bacilli, 58% of the respondents had answered correctly by mentioning lungs as the main part affected (Table 1). Regarding the transmission of tuberculosis 50% of the respondents knew correctly that TB is transmitted through droplet infection (Table 2). Knowledge on the clinical symptoms of tuberculosis, majority (82%) answered chronic cough, followed by fever (74%), blood in sputum (72%) loss of weight (50%) and loss of appetite (50%). This shows that two third of the respondent knew the common symptoms of Tuberculosis (Table 3).

On the knowledge about association of TB with HIV/AIDS only 16.6% knew that TB is the commonest opportunistic infection in people infected with HIV/AIDS (Table 4). More than two third of the respondents knew correctly that body secretion which contains TB bacilli is sputum (Table 5).

Knowledge on the suitable method for disposal of body fluids and sputum containing TB bacilli, only 30% knew the correctly that incineration was the suitable method of disposal (Table 6). On preventing the transmission of Tuberculosis 31.6% of the respondents felt that TB patients should use mask (Table 7).

Table 1: Parts of the body affected by TB bacilli

Parts of the body	Frequency	Percentage
Lung	174	58%
Chest	30	10%
Lung and liver	15	5%
Lung and chest	14	4.6%
Lung and skin	7	2.3%
Don't know	60	20%

Table 2: Mode of transmission of Tuberculosis

Mode of transmission	Frequency	Percentage
Droplet infection	150	50%
Coughing, sneezing and consuming food contaminated by TB patients	30	10%
Droplet infection and direct contact	28	9.3%
Droplet infection and use of materials contaminated by TB patients.	15	5%
Direct contact with TB patients	15	5%
Droplet infection and contaminated urine and stool	10	3.3%
Droplet infection and blood	10	3.3%
No idea	42	14%

Table 3: Clinical symptoms of Tuberculosis		
Clinical symptoms	**Frequency (300) for each symptom**	**Percentage**
I. Chronic cough	246	82%
II. Fever in the evening	222	74%
III. Blood in sputum	216	72%
IV. Loss of weight	150	50%
V. Loss of appetite	150	50%
VI. Chest pain	123	41%

Table 4: HIV and its relation with Tuberculosis		
HIV and its relation with tuberculosis	**Frequency**	**Percentage**
HIV is an un-curable disease and TB is curable disease	55	18.3%
TB is common opportunistic infection among HIV patients	50	16.6%
Mode of transmission of HIV is unsafe sexual contact and TB by droplet infection, smoking and alcohol drinking habit.	40	13.3%
No relation between TB and HIV	30	10%
Don't know any relation between TB and HIV	45	15%
Don't know about HIV	80	26.6%

Table 5: Body secretion where Tubercle bacilli are found		
Body secretion where tubercle bacilli are found	**Frequency**	**Percentage**
Sputum	160	53.3%
Sputum and saliva	33	11%
Sputum, saliva and urine	21	7%
Sputum, blood and saliva	20	6.6%
Sputum and stool	15	5%
Sputum, blood, saliva and urine	6	2%
Sputum, saliva, blood, urine and stool	6	2%
Urine and stool	6	2%
Don't know	33	11%

Table 6: Disposable method of Sputum and other Body fluids		
Disposable method	**Frequency**	**Percentage**
Digging	105	35%
Incineration and digging of sputum	39	13%
Incineration, digging and use of disinfectant	27	9%
Incineration	24	8%
Chemotherapy reduce infectivity	21	7%
Don't know	84	28%

Table 7: Preventive method of Tuberculosis Transmission		
Preventive method	**Frequency**	**Percentage**
TB patients should use mask	95	31.6%
Don't use TB patient's utensils and cloths	65	21.6%
Separate the TB patients from community	54	18%
TB patients should use mask and properly dispose patient's sputum and other materials	21	7%
Don't visit the TB patients	15	5%
TB patient should treat as early as possible	15	5%
Don't know	35	11.6%

DISCUSSION

The finding of this study showed that majority (73%) of the TB patients belong to the economically active young age group of 21-50 years, this finding is consistent with the earlier finding of Bam (2003).[17] where 95% of TB patients were in the age group of 15-54 years. This finding suggests that TB is common among the economically active group having direct impact to the family and the national economy. This finding also supports the global burden of TB in developing countries where 75% of cases are within

the economically and most productive age group (15-54 years).[15] This finding of the study also suggests that burden of TB will cause economic loss to the family and community in Nepal because it is found that an adult with TB, in the developing world loses on average 3-4 months of work time, 20%-30% of annual house hold income and 15 years income if patient dies causing staggering economic loss to the family and the community.[18]

More males (64%) were found to be suffering from TB compared to females (36%) this could be possible due to sampling bias where more males were included in the study then females, however this finding is consistent with earlier findings by Bam (65%) in (2003).[17] Low incidence of TB among females in this study could also be because of the low status accorded to women in Nepal where male domination still exists and women has limited decision making power, restricted mobility and poor access to basic and available health care. Women in Nepal may be more vulnerable to TB because of gender disparity that still exist giving women less opportunity for education, food and nutrition. On the other hand, the higher incidence of TB among man could be attributed to vulneralibity of men to TB because of their mobile life style and exposure to predisposing factors like smoking, alcohol, drug abuse.

Majority (58%) of respondents knew correctly that common part of the body infected by TB is the lungs and 53.3% of the participants of the survey responded correctly that TB bacilli are excreted in the sputum. But only 30% of them were aware that incineration is the appropriate way of disposition of sputum and other body fluids. Above findings are important for developing prevention strategies for TB because TB disease primarily affects lungs causing pulmonary tuberculosis[19, 20] and patient excreting TB bacilli in the sputum are the principal sources of infection.[23] People with prolonged, frequent, or intense contact are at particularly high risk of becoming infected, with an estimated 22% infection rate. A person with active but untreated tuberculosis can infect 10–15 other people per year.[21]

Knowledge on the transmission of tuberculosis showed that only 50% of patients knew that tuberculosis is infectious disease transmitted by droplet infection. Only 32% of respondent knew that use of mask by TB patient can prevent Tuberculosis. A similar study conduct by Joshi et al. (2006)[22] showed that out of 58 respondents 28 were of the view that to prevent the transmission of TB it is advised not to sleep in a common place and 32 said transmission could be prevented by covering their mouth while coughing. Above findings of this study suggests that more emphasis should be given on teaching patients on mode of transmission of TB bacilli and using mask to prevent transmission of TB, because use of face mask by TB patients decreases the risk of transmission of TB infection to others.

It had been found that majority of the respondents (82%) were aware of tuberculosis symptoms such as coughing (82%), fever in the evening (74%) and blood in sputum (72%). These findings are significant for future intervention in TB control because sociological studies carried out in India have shown that an overwhelming majority of patients of pulmonary tuberculosis have one or more of the symptoms referable to chest, such as persistent cough and fever, and many of them (over 60 per cent) seek medical advice on their own initiative. The chest symptoms often develop early, that is before the disease has gone on to an advanced stage.[23]

Knowledge of the surveyed population on the relationship of TB with HIV showed that only 16.6% of the respondents were aware that TB is common opportunistic infection among HIV patients. This finding suggests that the knowledge of the TB patient about TB and HIV co-infection is poor. Because the rate of progression to clinical TB disease is 10 to 30 times higher among individuals infected by both TB and HIV than among those infected only with TB. This is because people with HIV infection have suppressed immunity and hence chances of reactivation of dormant TB bacilli is many fold higher in them than among those without HIV. Moreover, due to low immunity, natural infection may rapidly lead to TB disease. Therefore, HIV infected persons are likely to get numerous opportunistic infections including TB. HIV is therefore considered the most important risk factor for TB in many countries. HIV is likely to worsen the TB situation in most countries with advanced HIV epidemic. Moreover, this may also contribute to an increase in drug resistance. The annual risk of developing TB in HIV infected individuals co-infected with MTB is 5-10%. Lifetime risk of development of active TB among co infected people (latent MTB and HIV) is 60% and among latent MTB infected individuals is 10%. TB is the most common causes of HIV related illness and death. HIV not only increases the number of TB cases, but also alters the clinical course of TB disease.[24]

CONCLUSION AND RECOMMENDATIONS

The finding of this study has found that respondents had adequate knowledge about the common signs and symptoms of Tuberculosis and more then 50% knew about

the common part of the body infected by TB bacilli. These are important findings because signs and symptoms are important for early diagnosis and treatment and reduce the spread of Tuberculosis in the community.

The surveyed population had less representation from the female gender so it is recommended that future studies may be carried out with equal representation from both sexes. On the mode of transmission only 50% knew correctly that it is transmitted by droplet infection, and few percentages of patients knew the other methods of transmission. It is recommended that emphasis should be given to improve the knowledge of the people on all the methods of TB transmission. Majority of the patients knew about the common clinical symptoms of TB like chronic cough (82%), fever in the evening (74%), blood in sputum (72%), this finding suggests that awareness to the patient on clinical feature of TB has been good.

Knowledge on the association of TB and HIV was low with only 16.6% responding that there is association between TB and HIV. It was also found that 26% of the patients did not know about HIV. This finding suggests that HIV/TB collaborative activities should be strengthened in order to increase the knowledge of patients on TB/HIV association. It is also recommended that such interventions should be targeted towards TB patients as well as HIV positive patients.

On Patient's knowledge on body secretion containing TB bacilli 53.3% answered correctly that sputum contains TB bacilli. Since TB is transmitted from sputum positive patients it is important that more awareness should be given on this subject.

The finding of the study on the knowledge of patients on proper disposal of sputum, it was observed that there was no significant positive finding. This suggests that more awareness should be given to patients on proper disposal so that transmission could be reduced.

Knowledge on the prevention of TB transmission, it was observed that only 31.6 % knew that TB patients should use mask, this may be because patients must be thinking of using a medical mask for prevention, so in future health education programs for patients it may be emphasized that covering of mouth while coughing and use of other forms of masks like handkerchief can also be used.

There were also important findings on the knowledge of patients on prevention where only 18% felt that TB patients should be separated from the community and 5% said not to visit TB patients. These findings suggest that patients had knowledge that TB patients should not be stigmatized.

Over all findings of the study suggests that health education and awareness program for TB patients should be strengthened and it should contain all aspect of the TB prevention. This study is done only in two centers so the findings and recommendations should not taken for the whole of Nepal. Further study is recommended to develop a general guideline for developing awareness campaign and health education for TB patients.

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Case Study

ALL MEMBERS OF A SINGLE FAMILY INCLUDING A 5-MONTHS OLD INFANT HAVING TUBERCULOSIS– A CASE REPORT

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ABSTRACT

Introduction : The incidence and number of tuberculosis (TB) cases have been increased dramatically all over the world. It is a major public health problem in Bangladesh too.

Case Summary : A 5-months old male infant, immunized as per EPI schedule, 3rd issue of a nonconsanguinous parents residence at downtown, Dhaka from a poor socioeconomic background was admitted into the Paediatrics ward, Bangladesh Medical College Hospital on 11th March 2004 with fever for 1 month, dry cough for 21 days, loose motion and vomiting for 14 days. He was weaned from breast milk at 3 months of his age and there was gross malfeeding history. BCG vaccine was given at 6 weeks. His mother had also been suffering from recurrent febrile illnesses and weight loss for many months. Baby was looking ill but conscious, mildly pale, afebrile with no dyspnoea. Z score of wt/age, lth/age, wt/lth and OFC were –2.9, -3.5, -0.3 and –0.3 respectively. Fontanel was open and normal. There was no lymphadenopathy and BCG mark was present. Breath sound was vesicular with fine crepitation on right lung. He was treated initially as septicemia by combined parenteral antibiotics. But response was not satisfactory. Lab data yielded raised ESR, eosinophillia, pyuria and haematuria with sterile culture. Chest X ray was abnormal. Mantoux Test (MT) was found strongly positive (18mm/72hrs.). Other family members were immediately screened for TB and all revealed positive. Complete Blood Count, MT and Chest X ray were chosen as screening methods for them. We treated with anti tubercular therapy to all of them including baby. We also corrected the feeding practice of the patient and kept in close monitoring. He showed remarkable clinical improvement with weight gaining. We discharged him as disseminated tuberculosis with having pulmonary tuberculosis among all other family members and advised for follow up. They all were cured. At present, they are healthy and baby is now 4 years of age with good physical and mental growth.

Conclusion : TB can mimic everything. A high index of suspicion by the clinician is essential for early diagnosis. Message: Family members of affected child must be screened for active TB

Keywords : Tuberculosis, Tuberculosis in infant, Pan family tuberculosis.

BACKGROUND

The incidence and number of tuberculosis (TB) cases have been increased dramatically. More than 8 million of new cases of TB occur and 3 million people die /year worldwide (WHO). Almost 1.3 million cases and 450,000 deaths occur in children per year.[1,2] It usually occurs in underdeveloped countries due to poverty, limitation in health-care services to high-risk populations. But in developed countries it is due to immigration from the prevalence countries and the epidemic of human immuno deficiency virus (HIV) infection. According to the WHO, developing countries including India, China, Pakistan, Philippines, Thailand, Indonesia, Bangladesh, and the Democratic Republic of Congo account for nearly 75% of all cases of TB.[3] TB is a major public health problem in Bangladesh. Over 300,000 people develop the disease every year of whom 70,000 die.[4]

TB equally affects both sexes and mortality exists at the extremes of age. Most children are infected with M.

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tuberculosis in their home by some one close to them. But they rarely infect other children or adults.[1]

Disseminated or meningeal tuberculosis are most fatal and are early manifestations, often occurring within 2-6 months of the infection.[1] The most clinically significant form of disseminated tuberculosis is milliary disease, which is most common in infants and young children. Because this form of tuberculosis is most common in infants and in malnourished or immunosuppresed patients, the host–immune in competency probably also plays a significant role in pathogenesis.[1]

CASE SUMMARY

Sayeed, 5-months, immunized as per EPI schedule, 3rd sib (out of 3) of a nonconsanguinous parents residence at slum area at downtown, Dhaka was admitted on 11th March 2004 with fever for 1 month, dry cough for 21 days, loose motion and vomiting for 14 days. Fever was low grade, occasionally become higher and mostly comes at night with profuse sweating. There was no history of convulsion, unconsciousness or ear discharge. For last 21 days along with fever he developed dry cough that was gradually deteriorating. He also developed loose motion for last 14 days that was very smelly but not bloody associated with vomiting containing food particles about 9-10 times / day. He was treated for several times by several antibiotics without any satisfactory result. Sayeed is borned normally at term in a clinic and cried just after birth. His mother was on regular antenatal care and her pregnancy was uneventful. He had history of early weaning from exclusive breast feeding within first 3 months of his age and replaced by formula as well as cows milk with feeder. He thrived well upto his first 3 months of age. BCG vaccine was given at 6 weeks. There was no history of contact with known case of TB patient although his mother had been suffering from recurrent febrile illnesses and weight loss for many months. Sayeed was looking ill but conscious, mildly pale, afebrile with no dyspnoea and facial dysmorphism. He was mildly dehydrated but not icteric, oedematous or cyanosed. His weight, supine length and OFC were 5.5kg, 59cm and 43cm respectively. Z score of wt/age, lth/age, wt/lth and OFC were –2.9, -3.5, -0.3 and –0.3 respectively. Fontanel was open and normal. Heart rate was 150/min and respiratory rate 32/min. There was no lymphadenopathy and BCG mark is present. Breath sound was vesicular with fine crepitation especially on right lung. Heart sounds were audible in all 4 areas with no murmur. All other systemic enquiry revealed normal. He was treated initially as septicemia by combined parenteral antibiotics covering gram-negative organism. But response was not satisfactory. Lab data yielded raised ESR (70mm), eosinophillia (5.0%), pyuria (50-60/HPF) and haematuria (10-20/HPF) with sterile culture. Chest X ray (A/P and Lateral view) revealed patchy densities along paracardiac as well as parahilar region on right side and also in left parahilar region. The radiological advice was to correlate clinically and laboratory findings to exclude tuberculosis. MT was done and response was much exaggerated with a reading of 18mm after 72hrs. All other members of his family were immediately screened for tuberculosis and revealed positive evidenced by MT (30mm, 28mm and 25mm after 72 hours found in father, mother and brother respectively) with raised ESR. Regarding chest X-ray, other than his brother (revealed right hilar lymph adenopathy and radiological advice was to exclude tuberculosis) all other family members found nothing significant abnormal findings. Except mother, rest of the family members was asymptomatic. But the patient's father was a smoker and had history of recurrent episodes of dry cough. We started anti tubercular therapy to all of them for 6 months and 12 months for Sayeed. We also corrected the feeding practice of the patient and kept in close monitoring. He showed remarkable improvement as he became playful, appetite increased; frequency of loose motion decreased and gained his weight from 5.5kg to 5.7kg. After 11 days of admission we discharged him as disseminated tuberculosis with having pulmonary tuberculosis among all other family members and advised for follow up. They all completed full course of drugs and became fully cured. At present they are healthy. Sayeed is now 4 years of age and his weight is 15kg (Median 16.5kg) and height is 98 cm (Median 102cm) with good physical and mental growth.

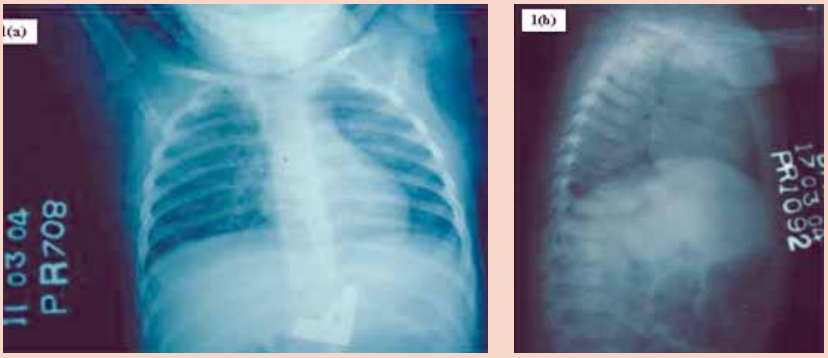

Figure 1(a,b): Chest X ray (A/P and Lateral view) of Sayeed

Figure 2: Positive induration of MT

Figure 3: Chest X ray of Father (a), Mother(b) and Brother(c)

Figure 4: Sayeed at 5 month of age (During admission & before treatment)

Figure 5: Sayeed with good physique (At present after treatment)

DISCUSSION :

The number of tuberculosis among infant is three times larger than those of one or two years old children because of their weak immune systems.[5,6]

Infants who have regular contact (such as living in the same house) with someone who has active (infectious) tuberculosis (TB) have an increased risk of becoming infected.[7] Our patient had a history of close contact with TB patients as all other of his family members were infected with TB.

Environmental factors also contribute to the likelihood of acquiring the infection. The concentration of bacilli depends on the ventilation of the surroundings and exposure to ultraviolet light. Thus, overcrowding, poor housing, and inadequate ventilation predispose individuals to the development of TB.[3] These were all present in our case.

The main determinant of the pathogenicity of TB is its ability to escape host defense mechanisms.[3,8]

Most infants with tuberculosis are symptomatic at the time of diagnosis, and bacteriologic confirmation was obtained in 70% of cases. A study in Texus done between 1985 and 1992 found Seventy-nine percent symptomatic when diagnosed, whereas most of the older children are not. The two most common symptoms were cough and fever. Fever usually low grade and comes at night, although could be as high as 39ºC and lasted for an average of 14 to 21 days. All fever had resolved in 98 percent of patients by 10 weeks.[9,10,11] But in another study done in South Africa, 2004 where 69.8% of cases were found asymptomatic at the time of screening[12]. Our patient was symptomatic at diagnosis and had similar pattern of fever for a month and cough as well. Moreover, our patient was malnourished and early weaned from breast milk (at 3 months); substituted by infant formula and cow's milk in a faulty way caused him more immunosuppressed and made vulnerable to develop TB. These may be the additional important causes to develop weight loss according to age, reluctant to feed and persistent diarrhoea.

Diagnosis of Disseminated TB in infants is difficult enough and a high index of suspicion is required. Bacteriologic confirmation is also very difficult and the tuberculin skin test is frequently negative in patients of this age group with Disseminated TB. The most important clue is history of contact to an adult with infectious tuberculosis[13]. We diagnosed our case from high index of suspicion and by clinical history that was supported by positive tuberculin test as well as abnormal chest X-ray. According to TB Score Chart for use in the Diagnosis of TB in Children Adopted from World Health Organization our patient scored '7' (as duration of illness more than 4 weeks, nutritional status – wt/age within 60%-80% and Positive Mantoux test scored 3, 1 and 3 respectively and collectively scored 7) indicates a high likelihood of TB, starting treatment is justified[14]. The presence of acid-fast-bacilli (AFB) on a sputum smear or other specimen often indicates TB disease. Although acid-fast microscopy is easy and quick, it does not confirm a diagnosis of TB because some acid-fast-bacilli are not M. tuberculosis. Culture can be done on all initial samples to confirm the diagnosis but a positive culture is not always necessary to begin or continue treatment for TB[15]. Moreover, the chance of AFB stain of urine is not so high and AFB culture and sensitivity is usually takes 6 weeks and is not available in our institute. As the condition of our patient was so critical and the antibiotic therapy failed, we resorted to antitubercular therapy (ATT) by clinical decision. The child responded promptly. So, we did not go for AFB stain and AFB culture and sensitivity of urine of our patient.

We also screened all other family members to find out any active TB and Complete Blood Count, MT and Chest X ray were chosen as screening methods. We could not do the sputum examination of patient's other family members due to their inconvenience. It may be our drawback but the TB is still considered as social curse by many families in Bangladesh. Parents especially father initially did not show any co-operation with us and even after our proper counseling for doing screening for tuberculosis, he was repeatedly refusing to give consent from doing so not only for himself but also for his spouse. After continuous counseling he at last gave consent for himself and for his wife and other sibs only for tuberculin test, blood count and chest X-ray.

Treatment is very difficult in infants having tuberculosis. One of major reasons is the rapid progress of the disease because of their underdeveloped cell-mediated immunity. Delay in the diagnosis also makes the treatment difficult. During treatment, systemic and enteric infections and liver functional disorders caused by these infections sometimes disturb the treatment for tuberculosis[5]. Fortunately, we did not find any such difficulties during the period of anti tubercular therapy (ATT) in our case. Probably early diagnosis and early initiation of ATT save the infant from facing various treatment related hazards. Moreover, family

members of our patient who had also TB did not suffer from any treatment induced complications too.

We commenced ATT as a traditional way and not as DOTS. We also corrected the feeding practice of the patient and kept in close monitoring. Although we could not show any bacteriological proof of having tuberculosis of our patient as well as his other family members and treated them with ATT on the basis of high index of suspicion and clinical history that was supported by some laboratory findings, we found satisfactory results evidenced by remarkable clinical improvement of our patient and his other family members as well. Tuberculosis is the disease where bacteriological proof is very difficult especially in children and all the diagnostic criteria cannot be fulfilled properly. If we do not go for ATT to a patient who actually has TB on the basis of high index suspicion due to lack of proof of bacteriological identification, it may be fatal.

CONCLUSION

TB can mimic any symptom and any sign. A high index of suspicion by the clinician is essential for early diagnosis. The prognosis is excellent if the diagnosis is made early and is often life saving.

MESSAGE

Family members of affected child must be screened for active TB.

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